```
GGCGGCCGCA GCCTCGGCTA CAGCTTCGGC GGCGAAGGTC AGCGCCGACG GCAGCCGGCA      60

CCTGACGGCG TGACCGACCC GAGCCGATTT CTCTTGGATT TGGCTACACA CTTATAGATC     120

TTCTGCACTG TTTACAGGCA CAGTTGCTGA TATGTGTTCA AG ATG AGT GGG ATG        174
                                               Met Ser Gly Met
                                                 1

GGA GAA AAT ACC TCT GAC CCC TCC AGG GCA GAG ACA AGA AAG CGC AAG       222
Gly Glu Asn Thr Ser Asp Pro Ser Arg Ala Glu Thr Arg Lys Arg Lys
  5                  10                  15                  20

GAA TGT CCT GAC CAA CTT GGA CCC AGC CCC AAA AGG AAC ACT GAA AAA       270
Glu Cys Pro Asp Gln Leu Gly Pro Ser Pro Lys Arg Asn Thr Glu Lys
                  25                  30                  35

CGT AAT CGT GAA CAG GAA AAT AAA TAT ATA GAA GAA CTT GCA GAG TTG       318
Arg Asn Arg Glu Gln Glu Asn Lys Tyr Ile Glu Glu Leu Ala Glu Leu
              40                  45                  50

ATT TTT GCA AAT TTT AAT GAT ATA GAC AAC TTT AAC TTC AAA CCT GAC       366
Ile Phe Ala Asn Phe Asn Asp Ile Asp Asn Phe Asn Phe Lys Pro Asp
          55                  60                  65

AAA TGT GCA ATC TTA AAA GAA ACT GTG AAG CAA ATT CGT CAG ATC AAA       414
Lys Cys Ala Ile Leu Lys Glu Thr Val Lys Gln Ile Arg Gln Ile Lys
     70                  75                  80

GAA CAA GAG AAA GCA GCA GCT GCC AAC ATA GAT GAA GTG CAG AAG TCA       462
Glu Gln Glu Lys Ala Ala Ala Ala Asn Ile Asp Glu Val Gln Lys Ser
 85                  90                  95                  100
```

FIG.1A

```
GAT GTA TCC TCT ACA GGG CAG GGT GTC ATC GAC AAG GAT GCG CTG GGG          510
Asp Val Ser Ser Thr Gly Gln Gly Val Ile Asp Lys Asp Ala Leu Gly
                105                 110                 115

CCT ATG ATG CTT GAG GCC CTT GAT GGG TTC TTC TTT GTA GTG AAC CTG          558
Pro Met Met Leu Glu Ala Leu Asp Gly Phe Phe Phe Val Val Asn Leu
            120                 125                 130

GAA GGC AAC GTT GTG TTT GTG TCA GAG AAT GTG ACA CAG TAT CTA AGG          606
Glu Gly Asn Val Val Phe Val Ser Glu Asn Val Thr Gln Tyr Leu Arg
        135                 140                 145

TAT AAC CAA GAA GAG CTG ATG AAC AAA AGT GTA TAT AGC ATC TTG CAT          654
Tyr Asn Gln Glu Glu Leu Met Asn Lys Ser Val Tyr Ser Ile Leu His
    150                 155                 160

GTT GGG GAC CAC ACG GAA TTT GTC AAA AAC CTG CTG CCA AAG TCT ATA          702
Val Gly Asp His Thr Glu Phe Val Lys Asn Leu Leu Pro Lys Ser Ile
165                 170                 175                 180

GTA AAT GGG GGA TCT TGG TCT GGC GAA CCT CCG AGG CGG AAC AGC CAT          750
Val Asn Gly Gly Ser Trp Ser Gly Glu Pro Pro Arg Arg Asn Ser His
                185                 190                 195

ACC TTC AAT TGT CGG ATG CTG GTA AAA CCT TTA CCT GAT TCA GAA GAG          798
Thr Phe Asn Cys Arg Met Leu Val Lys Pro Leu Pro Asp Ser Glu Glu
            200                 205                 210

GAG GGT CAT GAT AAC CAG GAA GCT CAT CAG AAA TAT GAA ACT ATG CAG          846
Glu Gly His Asp Asn Gln Glu Ala His Gln Lys Tyr Glu Thr Met Gln
        215                 220                 225
```

FIG.1B

```
TGC TTC GCT GTC TCT CAA CCA AAG TCC ATC AAA GAA GAA GGA GAA GAT          894
Cys Phe Ala Val Ser Gln Pro Lys Ser Ile Lys Glu Glu Gly Glu Asp
    230                 235                 240

TTG CAG TCC TGC TTG ATT TGC GTG GCA AGA AGA GTT CCC ATG AAG GAA          942
Leu Gln Ser Cys Leu Ile Cys Val Ala Arg Arg Val Pro Met Lys Glu
245                 250                 255                 260

AGA CCA GTT CTT CCC TCA TCA GAA AGT TTT ACT ACT CGC CAG GAT CTC          990
Arg Pro Val Leu Pro Ser Ser Glu Ser Phe Thr Thr Arg Gln Asp Leu
                265                 270                 275

CAA GGC AAG ATC ACG TCT CTG GAT ACC AGC ACC ATG AGA GCA GCC ATG         1038
Gln Gly Lys Ile Thr Ser Leu Asp Thr Ser Thr Met Arg Ala Ala Met
            280                 285                 290

AAA CCA GGC TGG GAG GAC CTG GTA AGA AGG TGT ATT CAG AAG TTC CAT         1086
Lys Pro Gly Trp Glu Asp Leu Val Arg Arg Cys Ile Gln Lys Phe His
        295                 300                 305

GCG CAG CAT GAA GGA GAA TCT GTG TCC TAT GCT AAG AGG CAT CAT CAT         1134
Ala Gln His Glu Gly Glu Ser Val Ser Tyr Ala Lys Arg His His His
    310                 315                 320

GAA GTA CTG AGA CAA GGA TTG GCA TTC AGT CAA ATC TAT CGT TTT TCC         1182
Glu Val Leu Arg Gln Gly Leu Ala Phe Ser Gln Ile Tyr Arg Phe Ser
325                 330                 335                 340

TTG TCT GAT GGC ACT CTT GTT GCT GCA CAA ACG AAG AGC AAA CTC ATC         1230
Leu Ser Asp Gly Thr Leu Val Ala Ala Gln Thr Lys Ser Lys Leu Ile
                345                 350                 355
```

FIG.1C

```
CGT TCT CAG ACT ACT AAT GAA CCT CAA CTT GTA ATA TCT TTA CAT ATG      1278
Arg Ser Gln Thr Thr Asn Glu Pro Gln Leu Val Ile Ser Leu His Met
            360                 365                 370

CTT CAC AGA GAG CAG AAT GTG TGT GTG ATG AAT CCG GAT CTG ACT GGA      1326
Leu His Arg Glu Gln Asn Val Cys Val Met Asn Pro Asp Leu Thr Gly
        375                 380                 385

CAA ACG ATG GGG AAG CCA CTG AAT CCA ATT AGC TCT AAC AGC CCT GCC      1374
Gln Thr Met Gly Lys Pro Leu Asn Pro Ile Ser Ser Asn Ser Pro Ala
    390                 395                 400

CAT CAG GCC CTG TGC AGT GGG AAC CCA GGT CAG GAC ATG ACC CTC AGT      1422
His Gln Ala Leu Cys Ser Gly Asn Pro Gly Gln Asp Met Thr Leu Ser
405                 410                 415                 420

AGC AAT ATA AAT TTT CCC ATA AAT GGC CCA AAG GAA CAA ATG GGC ATG      1470
Ser Asn Ile Asn Phe Pro Ile Asn Gly Pro Lys Glu Gln Met Gly Met
                425                 430                 435

CCC ATG GGC AGG TTT GGT GGT TCT GGG GGA ATG AAC CAT GTG TCA GGC      1518
Pro Met Gly Arg Phe Gly Gly Ser Gly Gly Met Asn His Val Ser Gly
            440                 445                 450

ATG CAA GCA ACC ACT CCT CAG GGT AGT AAC TAT GCA CTC AAA ATG AAC      1566
Met Gln Ala Thr Thr Pro Gln Gly Ser Asn Tyr Ala Leu Lys Met Asn
        455                 460                 465

AGC CCC TCA CAA AGC AGC CCT GGC ATG AAT CCA GGA CAG CCC ACC TCC      1614
Ser Pro Ser Gln Ser Ser Pro Gly Met Asn Pro Gly Gln Pro Thr Ser
    470                 475                 480
```

FIG.1D

```
ATG CTT TCA CCA AGG CAT CGC ATG AGC CCT GGA GTG GCT GGC AGC CCT      1662
Met Leu Ser Pro Arg His Arg Met Ser Pro Gly Val Ala Gly Ser Pro
485                 490                 495                 500

CGA ATC CCA CCC AGT CAG TTT TCC CCT GCA GGA AGC TTG CAT TCC CCT      1710
Arg Ile Pro Pro Ser Gln Phe Ser Pro Ala Gly Ser Leu His Ser Pro
                505                 510                 515

GTG GGA GTT TGC AGC AGC ACA GGA AAT AGC CAT AGT TAT ACC AAC AGC      1758
Val Gly Val Cys Ser Ser Thr Gly Asn Ser His Ser Tyr Thr Asn Ser
            520                 525                 530

TCC CTC AAT GCA CTT CAG GCC CTC AGC GAG GGG CAC GGG GTC TCA TTA      1806
Ser Leu Asn Ala Leu Gln Ala Leu Ser Glu Gly His Gly Val Ser Leu
        535                 540                 545

GGG TCA TCG TTG GCT TCA CCA GAC CTA AAA ATG GGC AAT TTG CAA AAC      1854
Gly Ser Ser Leu Ala Ser Pro Asp Leu Lys Met Gly Asn Leu Gln Asn
    550                 555                 560

TCC CCA GTT AAT ATG AAT CCT CCC CCA CTC AGC AAG ATG GGA AGC TTG      1902
Ser Pro Val Asn Met Asn Pro Pro Pro Leu Ser Lys Met Gly Ser Leu
565                 570                 575                 580

GAC TCA AAA GAC TGT TTT GGA CTA TAT GGG GAG CCC TCT GAA GGT ACA      1950
Asp Ser Lys Asp Cys Phe Gly Leu Tyr Gly Glu Pro Ser Glu Gly Thr
                585                 590                 595

ACT GGA CAA GCA GAG AGC AGC TGC CAT CCT GGA GAG CAA AAG GAA ACA      1998
Thr Gly Gln Ala Glu Ser Ser Cys His Pro Gly Glu Gln Lys Glu Thr
            600                 605                 610
```

FIG.1E

```
AAT GAC CCC AAC CTG CCC CCG GCC GTG AGC AGT GAG AGA GCT GAC GGG      2046
Asn Asp Pro Asn Leu Pro Pro Ala Val Ser Ser Glu Arg Ala Asp Gly
        615                 620                 625

CAG AGC AGA CTG CAT GAC AGC AAA GGG CAG ACC AAA CTC CTG CAG CTG      2094
Gln Ser Arg Leu His Asp Ser Lys Gly Gln Thr Lys Leu Leu Gln Leu
    630                 635                 640

CTG ACC ACC AAA TCT GAT CAG ATG GAG CCC TCG CCC TTA GCC AGC TCT      2142
Leu Thr Thr Lys Ser Asp Gln Met Glu Pro Ser Pro Leu Ala Ser Ser
645                 650                 655                 660

TTG TCG GAT ACA AAC AAA GAC TCC ACA GGT AGC TTG CCT GGT TCT GGG      2190
Leu Ser Asp Thr Asn Lys Asp Ser Thr Gly Ser Leu Pro Gly Ser Gly
                665                 670                 675

TCT ACA CAT GGA ACC TCG CTC AAG GAG AAG CAT AAA ATT TTG CAC AGA      2238
Ser Thr His Gly Thr Ser Leu Lys Glu Lys His Lys Ile Leu His Arg
            680                 685                 690

CTC TTG CAG GAC AGC AGT TCC CCT GTG GAC TTG GCC AAG TTA ACA GCA      2286
Leu Leu Gln Asp Ser Ser Ser Pro Val Asp Leu Ala Lys Leu Thr Ala
        695                 700                 705

GAA GCC ACA GGC AAA GAC CTG AGC CAG GAG TCC AGC AGC ACA GCT CCT      2334
Glu Ala Thr Gly Lys Asp Leu Ser Gln Glu Ser Ser Ser Thr Ala Pro
    710                 715                 720

GGA TCA GAA GTG ACT ATT AAA CAA GAG CCG GTG AGC CCC AAG AAG AAA      2382
Gly Ser Glu Val Thr Ile Lys Gln Glu Pro Val Ser Pro Lys Lys Lys
725                 730                 735                 740
```

FIG. 1F

```
GAG AAT GCA CTA CTT CGC TAT TTG CTA GAT AAA GAT GAT ACT AAA GAT      2430
Glu Asn Ala Leu Leu Arg Tyr Leu Leu Asp Lys Asp Asp Thr Lys Asp
                745                 750                 755

ATT GGT TTA CCA GAA ATA ACC CCC AAA CTT GAG AGA CTG GAC AGT AAG      2478
Ile Gly Leu Pro Glu Ile Thr Pro Lys Leu Glu Arg Leu Asp Ser Lys
            760                 765                 770

ACA GAT CCT GCC AGT AAC ACA AAA TTA ATA GCA ATG AAA ACT GAG AAG      2526
Thr Asp Pro Ala Ser Asn Thr Lys Leu Ile Ala Met Lys Thr Glu Lys
        775                 780                 785

GAG GAG ATG AGC TTT GAG CCT GGT GAC CAG CCT GGC AGT GAG CTG GAC      2574
Glu Glu Met Ser Phe Glu Pro Gly Asp Gln Pro Gly Ser Glu Leu Asp
    790                 795                 800

AAC TTG GAG GAG ATT TTG GAT GAT TTG CAG AAT AGT CAA TTA CCA CAG      2622
Asn Leu Glu Glu Ile Leu Asp Asp Leu Gln Asn Ser Gln Leu Pro Gln
805                 810                 815                 820

CTT TTC CCA GAC ACG AGG CCA GGC GCC CCT GCT GGA TCA GTT GAC AAG      2670
Leu Phe Pro Asp Thr Arg Pro Gly Ala Pro Ala Gly Ser Val Asp Lys
                825                 830                 835

CAA GCC ATC ATC AAT GAC CTC ATG CAA CTC ACA GCT GAA AAC AGC CCT      2718
Gln Ala Ile Ile Asn Asp Leu Met Gln Leu Thr Ala Glu Asn Ser Pro
            840                 845                 850

GTC ACA CCT GTT GGA GCC CAG AAA ACA GCA CTG CGA ATT TCA CAG AGC      2766
Val Thr Pro Val Gly Ala Gln Lys Thr Ala Leu Arg Ile Ser Gln Ser
        855                 860                 865
```

FIG.1G

```
ACT TTT AAT AAC CCA CGA CCA GGG CAA CTG GGC AGG TTA TTG CCA AAC      2814
Thr Phe Asn Asn Pro Arg Pro Gly Gln Leu Gly Arg Leu Leu Pro Asn
    870                 875                 880

CAG AAT TTA CCA CTT GAC ATC ACA TTG CAA AGC CCA ACT GGT GCT GGA      2862
Gln Asn Leu Pro Leu Asp Ile Thr Leu Gln Ser Pro Thr Gly Ala Gly
885                 890                 895                 900

CCT TTC CCA CCA ATC AGA AAC AGT AGT CCC TAC TCA GTG ATA CCT CAG      2910
Pro Phe Pro Pro Ile Arg Asn Ser Ser Pro Tyr Ser Val Ile Pro Gln
                905                 910                 915

CCA GGA ATG ATG GGT AAT CAA GGG ATG ATA GGA AAC CAA GGA AAT TTA      2958
Pro Gly Met Met Gly Asn Gln Gly Met Ile Gly Asn Gln Gly Asn Leu
            920                 925                 930

GGG AAC AGT AGC ACA GGA ATG ATT GGT AAC AGT GCT TCT CGG CCT ACT      3006
Gly Asn Ser Ser Thr Gly Met Ile Gly Asn Ser Ala Ser Arg Pro Thr
        935                 940                 945

ATG CCA TCT GGA GAA TGG GCA CCG CAG AGT TCG GCT GTG AGA GTC ACC      3054
Met Pro Ser Gly Glu Trp Ala Pro Gln Ser Ser Ala Val Arg Val Thr
    950                 955                 960

TGT GCT GCT ACC ACC AGT GCC ATG AAC CGG CCA GTC CAA GGA GGT ATG      3102
Cys Ala Ala Thr Thr Ser Ala Met Asn Arg Pro Val Gln Gly Gly Met
965                 970                 975                 980

ATT CGG AAC CCA GCA GCC AGC ATC CCC ATG AGG CCC AGC AGC CAG CCT      3150
Ile Arg Asn Pro Ala Ala Ser Ile Pro Met Arg Pro Ser Ser Gln Pro
                985                 990                 995
```

FIG.1H

```
GGC CAA AGA CAG ACG CTT CAG TCT CAG GTC ATG AAT ATA GGG CCA TCT      3198
Gly Gln Arg Gln Thr Leu Gln Ser Gln Val Met Asn Ile Gly Pro Ser
            1000                1005                1010

GAA TTA GAG ATG AAC ATG GGG GGA CCT CAG TAT AGC CAA CAA CAA GCT      3246
Glu Leu Glu Met Asn Met Gly Gly Pro Gln Tyr Ser Gln Gln Gln Ala
        1015                1020                1025

CCT CCA AAT CAG ACT GCC CCA TGG CCT GAA AGC ATC CTG CCT ATA GAC      3294
Pro Pro Asn Gln Thr Ala Pro Trp Pro Glu Ser Ile Leu Pro Ile Asp
    1030                1035                1040

CAG GCG TCT TTT GCC AGC CAA AAC AGG CAG CCA TTT GGC AGT TCT CCA      3342
Gln Ala Ser Phe Ala Ser Gln Asn Arg Gln Pro Phe Gly Ser Ser Pro
1045                1050                1055                1060

GAT GAC TTG CTA TGT CCA CAT CCT GCA GCT GAG TCT CCG AGT GAT GAG      3390
Asp Asp Leu Leu Cys Pro His Pro Ala Ala Glu Ser Pro Ser Asp Glu
                1065                1070                1075

GGA GCT CTC CTG GAC CAG CTG TAT CTG GCC TTG CGG AAT TTT GAT GGC      3438
Gly Ala Leu Leu Asp Gln Leu Tyr Leu Ala Leu Arg Asn Phe Asp Gly
            1080                1085                1090

CTG GAG GAG ATT GAT AGA GCC TTA GGA ATA CCC GAA CTG GTC AGC CAG      3486
Leu Glu Glu Ile Asp Arg Ala Leu Gly Ile Pro Glu Leu Val Ser Gln
        1095                1100                1105

AGC CAA GCA GTA GAT CCA GAA CAG TTC TCA AGT CAG GAT TCC AAC ATC      3534
Ser Gln Ala Val Asp Pro Glu Gln Phe Ser Ser Gln Asp Ser Asn Ile
    1110                1115                1120
```

FIG.1I

```
ATG CTG GAG CAG AAG GCG CCC GTT TTC CCA CAG CAG TAT GCA TCT CAG      3582
Met Leu Glu Gln Lys Ala Pro Val Phe Pro Gln Gln Tyr Ala Ser Gln
1125                1130                1135                1140

GCA CAA ATG GCC CAG GGT AGC TAT TCT CCC ATG CAA GAT CCA AAC TTT      3630
Ala Gln Met Ala Gln Gly Ser Tyr Ser Pro Met Gln Asp Pro Asn Phe
                1145                1150                1155

CAC ACC ATG GGA CAG CGG CCT AGT TAT GCC ACA CTC CGT ATG CAG CCC      3678
His Thr Met Gly Gln Arg Pro Ser Tyr Ala Thr Leu Arg Met Gln Pro
            1160                1165                1170

AGA CCG GGC CTC AGG CCC ACG GGC CTA GTG CAG AAC CAG CCA AAT CAA      3726
Arg Pro Gly Leu Arg Pro Thr Gly Leu Val Gln Asn Gln Pro Asn Gln
        1175                1180                1185

CTA AGA CTT CAA CTT CAG CAT CGC CTC CAA GCA CAG CAG AAT CGC CAG      3774
Leu Arg Leu Gln Leu Gln His Arg Leu Gln Ala Gln Gln Asn Arg Gln
    1190                1195                1200

CCA CTT ATG AAT CAA ATC AGC AAT GTT TCC AAT GTG AAC TTG ACT CTG      3822
Pro Leu Met Asn Gln Ile Ser Asn Val Ser Asn Val Asn Leu Thr Leu
1205                1210                1215                1220

AGG CCT GGA GTA CCA ACA CAG GCA CCT ATT AAT GCA CAG ATG CTG GCC      3870
Arg Pro Gly Val Pro Thr Gln Ala Pro Ile Asn Ala Gln Met Leu Ala
                1225                1230                1235

CAG AGA CAG AGG GAA ATC CTG AAC CAG CAT CTT CGA CAG AGA CAA ATG      3918
Gln Arg Gln Arg Glu Ile Leu Asn Gln His Leu Arg Gln Arg Gln Met
            1240                1245                1250
```

FIG. 1J

```
CAT CAG CAA CAG CAA GTT CAG CAA CGA ACT TTG ATG ATG AGA GGA CAA      3966
His Gln Gln Gln Gln Val Gln Gln Arg Thr Leu Met Met Arg Gly Gln
        1255                1260                1265

GGG TTG AAT ATG ACA CCA AGC ATG GTG GCT CCT AGT GGT ATG CCA GCA      4014
Gly Leu Asn Met Thr Pro Ser Met Val Ala Pro Ser Gly Met Pro Ala
    1270                1275                1280

ACT ATG AGC AAC CCT CGG ATT CCC CAG GCA AAT GCA CAG CAG TTT CCA      4062
Thr Met Ser Asn Pro Arg Ile Pro Gln Ala Asn Ala Gln Gln Phe Pro
1285                1290                1295                1300

TTT CCT CCA AAC TAC GGA ATA AGT CAG CAA CCT GAT CCA GGC TTT ACT      4110
Phe Pro Pro Asn Tyr Gly Ile Ser Gln Gln Pro Asp Pro Gly Phe Thr
                1305                1310                1315

GGG GCT ACG ACT CCC CAG AGC CCA CTT ATG TCA CCC CGA ATG GCA CAT      4158
Gly Ala Thr Thr Pro Gln Ser Pro Leu Met Ser Pro Arg Met Ala His
            1320                1325                1330

ACA CAG AGT CCC ATG ATG CAA CAG TCT CAG GCC AAC CCA GCC TAT CAG      4206
Thr Gln Ser Pro Met Met Gln Gln Ser Gln Ala Asn Pro Ala Tyr Gln
        1335                1340                1345

GCC CCC TCC GAC ATA AAT GGA TGG GCG CAG GGG AAC ATG GGC GGA AAC      4254
Ala Pro Ser Asp Ile Asn Gly Trp Ala Gln Gly Asn Met Gly Gly Asn
    1350                1355                1360

AGC ATG TTT TCC CAG CAG TCC CCA CCA CAC TTT GGG CAG CAA GCA AAC      4302
Ser Met Phe Ser Gln Gln Ser Pro Pro His Phe Gly Gln Gln Ala Asn
1365                1370                1375                1380
```

FIG.1K

```
ACC AGC ATG TAC AGT AAC AAC ATG AAC ATC AAT GTG TCC ATG GCG ACC      4350
Thr Ser Met Tyr Ser Asn Asn Met Asn Ile Asn Val Ser Met Ala Thr
                1385                1390                1395

AAC ACA GGT GGC ATG AGC AGC ATG AAC CAG ATG ACA GGA CAG ATC AGC      4398
Asn Thr Gly Gly Met Ser Ser Met Asn Gln Met Thr Gly Gln Ile Ser
            1400                1405                1410

ATG ACC TCA GTG ACC TCC GTG TCT ACG TCA GGG CTG TCC TCC ATG GGT      4446
Met Thr Ser Val Thr Ser Val Ser Thr Ser Gly Leu Ser Ser Met Gly
        1415                1420                1425

CCC GAG CAG GTT AAT GAT CCT GCT CTG AGG GGA GGC AAC CTG TTC CCA      4494
Pro Glu Gln Val Asn Asp Pro Ala Leu Arg Gly Gly Asn Leu Phe Pro
    1430                1435                1440

AAC CAG CTG CCT GGA ATG GAT ATG ATT AAG CAG GAG GGA GAC ACA ACA      4542
Asn Gln Leu Pro Gly Met Asp Met Ile Lys Gln Glu Gly Asp Thr Thr
1445                1450                1455                1460

CGG AAA TAT TGC TGACACTGCT GAAGCCAGTT GCTTCTTCAG CTGACCGGGC          4594
Arg Lys Tyr Cys

TCACTTGCTC AAAACACTTC CAGTCTGGAG AGCTGTGTCT ATTTGTTTCA ACCCAACTGA    4654

CCTGCCAGCC GGTTCTGCTA GAGCAGACAG GCCTGGCCCT GGTTCCCAGG GTGGCGTCCA    4714

CTCGGCTGTG GCAGGAGGAG CTGCCTCTTC TCTTGACAGT CTGAAGCTCG CATCCAGACA    4774

GTCGCTCAGT CTGTTCCCTG CATTCACCTT AGTGCAACTT AGATCTCTCC TCCCCAAGTA    4834
```

FIG. 1L

AATGTTGACA GGCCAATTTC ATACCCATGT CAGATTGAAT GTATTTAAAT GTATGTATTT 4894

AAGGAGAACC ATGCTCTTGT TCTGTTCCTG TTCGGTTCCA GACACTGGTT TCTTGCTTTG 4954

TTTTCCCTGG CTAACAGTCT AGTGCCAAAG ATTAAGATTT TATCTGGGGG AAAGAAAAGA 5014

ATTTTTTAAA AAATTAAACT AAAGATGTTT TAAGCTAAAG CCTGAATTTG GGATGGAAGC 5074

AGGACAGACA CCGTGGACAG CGCTGTATTT ACAGACACAC CCAGTGCGTG AAGACCAACA 5134

AAGTCACAGT CGTATCTCTA GAAAGCTCTA AAGACCATGT TGGAAAGAGT CTCCAGTTAC 5194

TGAACAGATG AAAAGGAGCC TGTGAGAGGG CTGTTAACAT TAGCAAATAT TTTTTCCTTG 5254

TTTTTTCTTT GTTAAAACCA AACTGGTTCA CCTGAATCAT GAATTGAGAA GAAATAATTT 5314

TCATTTCTAA ATTAAGTCCC TTTTAGTTTG ATCAGACAGC TTGAATCAGC ATCTCTTCTT 5374

CCCTGTCAGC CTGACTCTTC CCTTCCCCTC TCTCATTCCC CATACTCCCT ATTTTCATTC 5434

CTTTTTTAAA AAATAATATA AGCTACAGAA ACCAGGTAAG CCCTTTATTT CCTTAAATGT 5494

TTTGCCAGCC ACTTACCAAT TGCTAAGTAT TGAATTTCAG AAAAAAAAAA TGCATTTACT 5554

GGCAAGGAGA AGAGCAAAGT TAAGGCTTGA TACCAATCGA GCTAAGGATA CCTGCTTTGG 5614

AAGCATGTTT ATTCTGTTCC CCAGCAACTC TGGCCTCCAA AATGGGAGAA ACGCCAGTGT 5674

GTTTAAATTG ATAGCAGATA TCACGACAGA TTTAACCTCT GCCATGTGTT TTTTATTTTG 5734

TTTTTTAGCA GTGCTGACTA AGCCGAAGTT TTGTAAGGTA CATAAAATCC AATTTATATG 5794

FIG.1M

TAAACAAGCA ATAATTTAAG TTGAGAACTT ATGTGTTTTA ATTGTATAAT TTTTGTGAGG 5854

TATACATATT GTGGAATTGA CTCAAAAATG AGGTACTTCA GTATTAAATT AGATATCTTC 5914

ATAGCAATGT CTCCTAAAGG TGTTTTGTAA AGGATATCAA TGCCTTGATT AGACCTAATT 5974

TGTAGACTTA AGACTTTTTA TTTTCTAAAC CTTGTGATTC TGCTTATAAG TCATTTATCT 6034

AATCTATATG ATATGCAGCC GCTGTAGGAA CCAATTCTTG ATTTTTATAT GTTTATATTC 6094

TTTCTTAATG AACCTTAGAA AGACTACATG TTACTAAGCA GGCCACTTTT ATGGTTGTTT 6154

TT 6156

FIG.1N

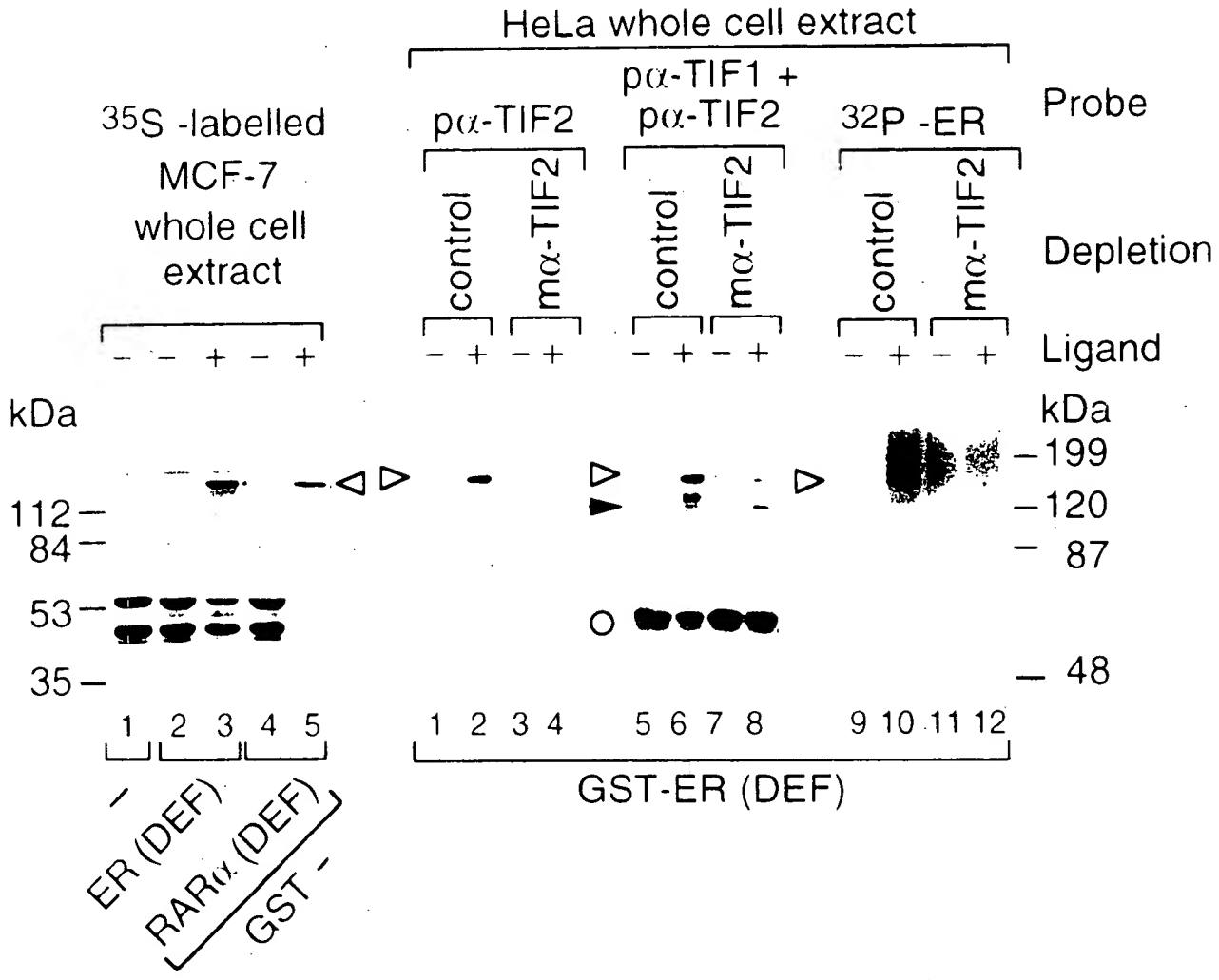

FIG.2A

FIG.2B

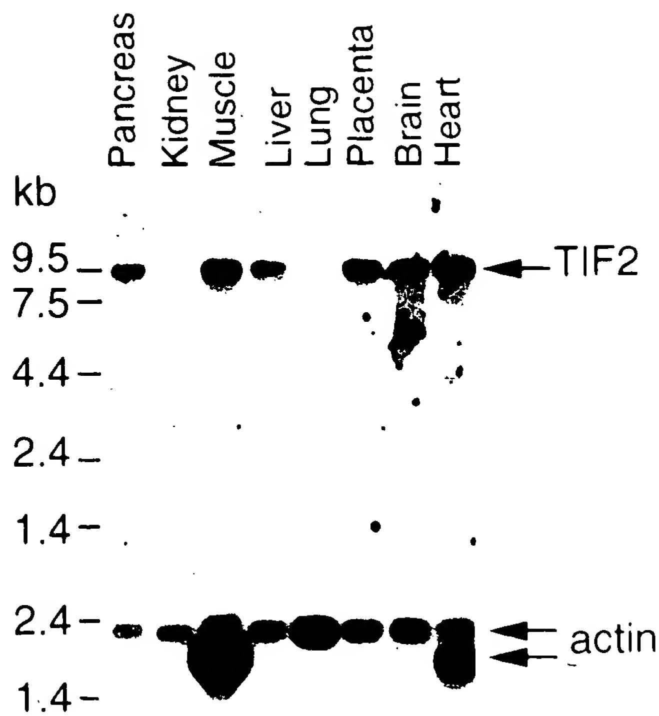
Pancreas
Kidney
Muscle
Liver
Lung
Placenta
Brain
Heart
kb
9.5
7.5
4.4
2.4
1.4
TIF2
2.4
1.4
actin

FIG.2C

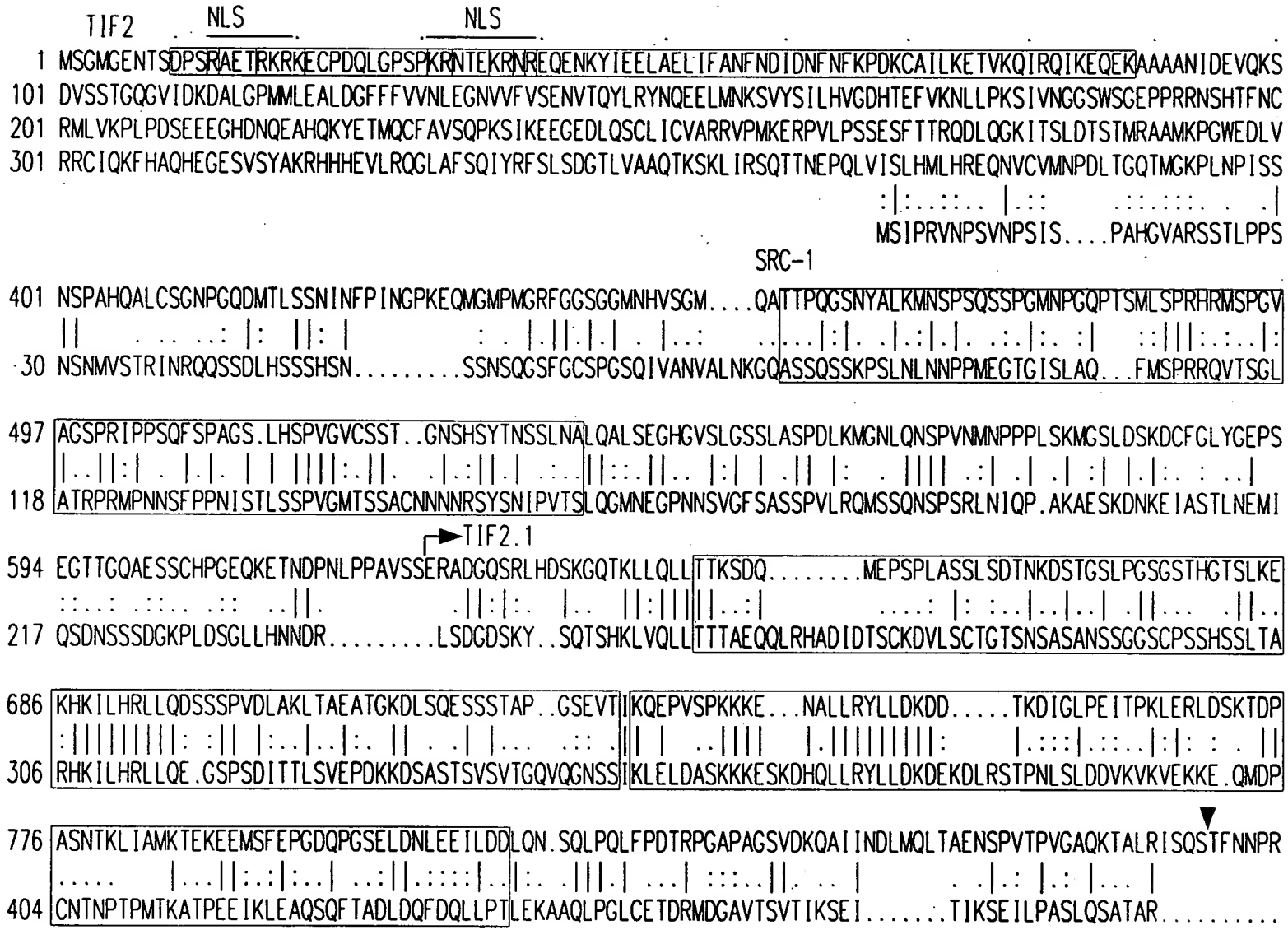

FIG.3A


875 PGQLGRLLPNQNLPLDITLQSPTGAGPFPPIRNSSPYSVIPQPGMMGNQGMIGNQGNLGNSSTGMIGNSASRPTMPSGEWAPQSSAVRVTCAATTSAMNR
481 .....PTSRLNR
975 PVQGGMIRNPAASIPMRPSSQPGQRQTLQSQVMNIGPSELEMNMGGPQYSQQQAPPNQTAPWPESILPIDQASFASQNRQPFGSSPDDLLCPHPAAESPS
488 .....LPELELEAIDNQFG.QPGTGDQIPWTNNTVTAINQ...SKSEDQCISSQLDELLCPPTTVEGRN
1075 DEGALLDQL..YLALRNFDGLEEIDRALGIPELV.SQSQAVDPEQFSSQDSN..IMLEQKAPVFPQQYASQAQMAQGSYSPMQDPNFHTMGQRPSYATLR
548 DEKALLEQLVSFLSGKDETELAELDRALGIDKLVQGGGLDVLSERFPPQQATPPLIMEERPNLYSQPYSSPFPTANLP.SPFQG....MVRQKPSLGTMP
1170 MQ...PRPGLRPTGLVQ.....NQPNQLRLQLQHRLQAQ.....QNRQPLMNQISNVSNVNLTLRPG....VPTQAPINAQMLAQRQREILNQHLR
643 VQVTPPRGAFSPGMGMQPRQTLNRPPAAPNQLRLQLQQRLQGQQQLIHQNRQAILNQFAATAPVGINMRSGMQQQITPQPPLNAQMLAQRQRELYSQQHR
TIF2.1
1249 QRQMHQQQQVQQRTLMMRGQGLNMTPSMVAPSGMPATMSNPRIPQANAQQFFPPPNYG.....
743 QRQLIQ....QQRAMLMRQQSF..GNNLPPSSGLPVQTGNPRLPQGAPQQFPYPPNYGTNPGTPPASTSPFSQLAANPEASLANRNSMVSRGMTGNIGGQ
1307 .....ISQQPDPGFTGATTPQSPLMSPRMAHTQSPMMQQSQANPAYQAPSDINGWAQGNMSGGNSMFQQSPPHFGQQANTSMYSN
837 FGTGINPQMQQNVFQYPGAGMVPQGEANFAPSLSPGSSMVPMPIPPPQSSLLQQTPPASGYQSP.DMKAWQQGAIGNNNVFSQAVQNQ.PTPAQPGVY.N
dnSRC-1
1387 NMNINVSMATNTGGMSSMNQMTGQISMTSVTSVSTSGLSSMGPEQVNDPALRGGNLFPNQLPGMDMIKQEGDTTRKYC*
934 NMSITVSMAGGNTNVQNMNPMMAQMQM...SSLQMPGMNTVCPEQINDPALRHTGLYCNQLSSTDLLKTEADGTQQVQQVQVFADVQCTVNLVGGDPYLN

FIG.3B

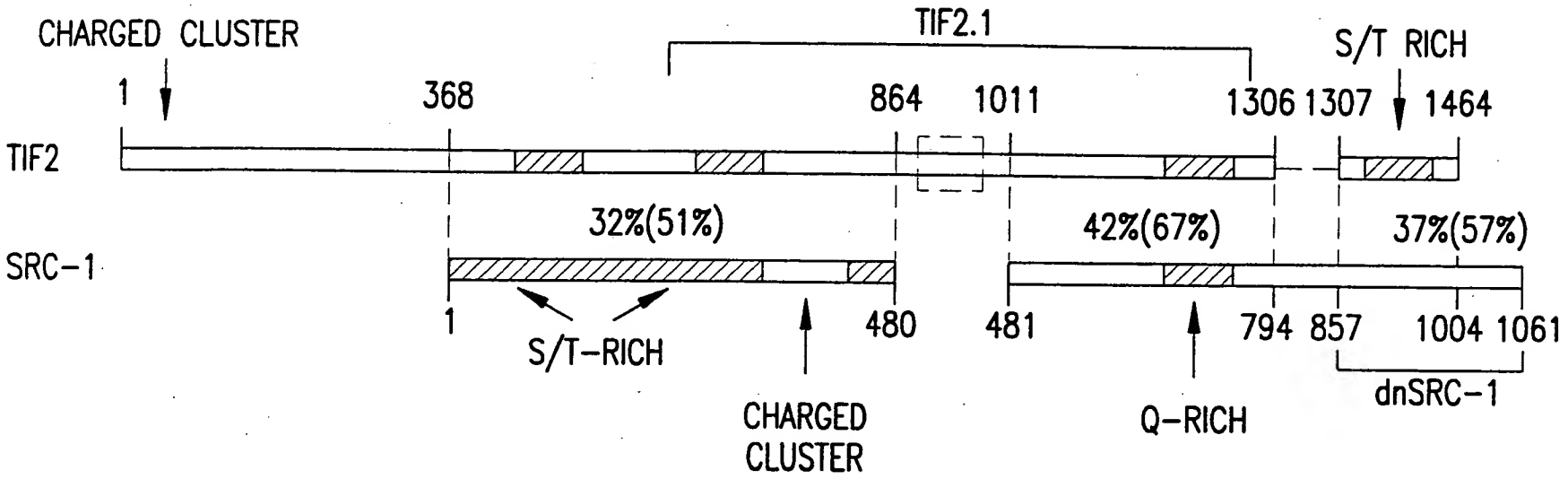

FIG.3C

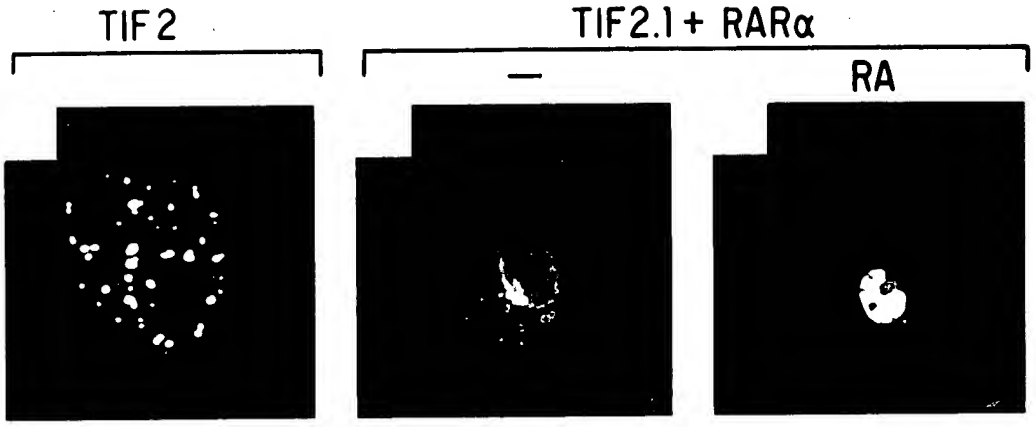

FIG.4A FIG.4B FIG.4C

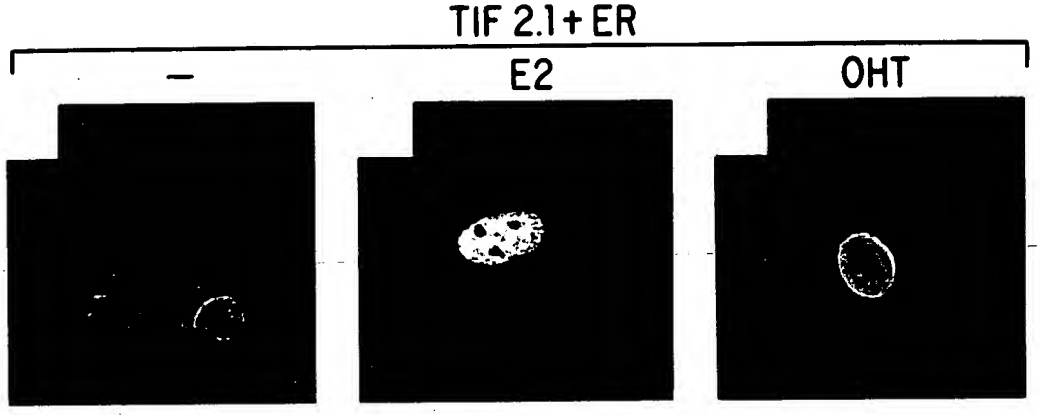

FIG.4D FIG.4E FIG.4F

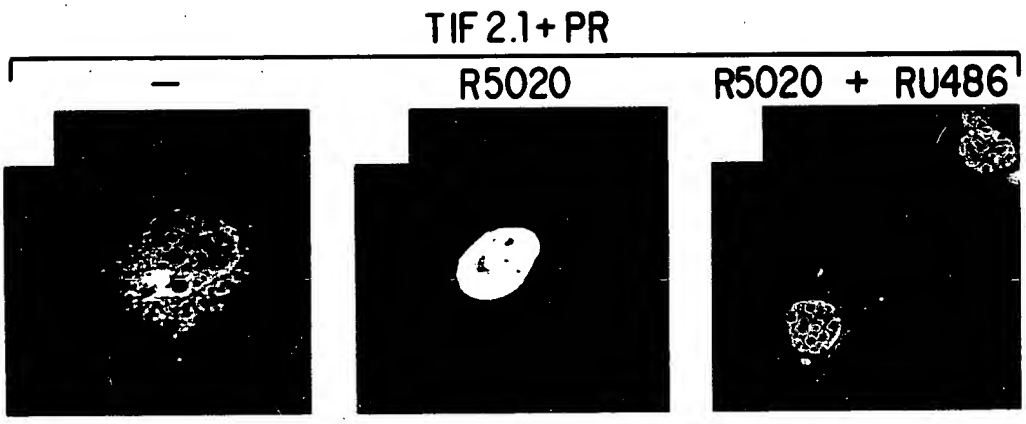

FIG.4G FIG.4H FIG.4I

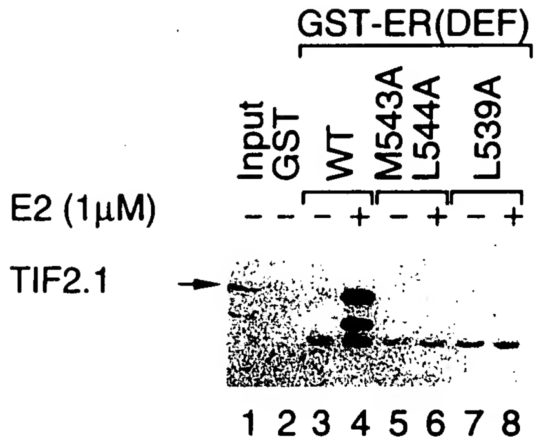

FIG.4K

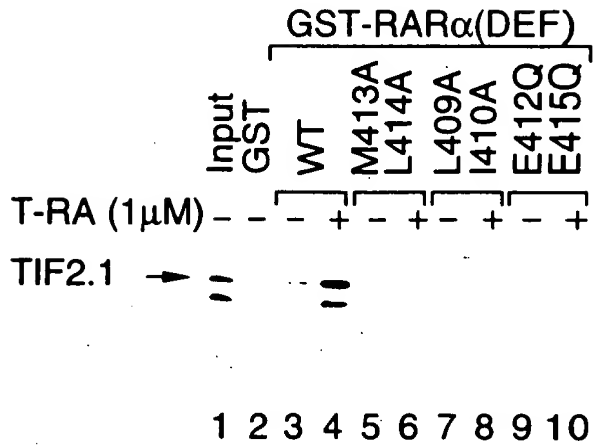

FIG.4L

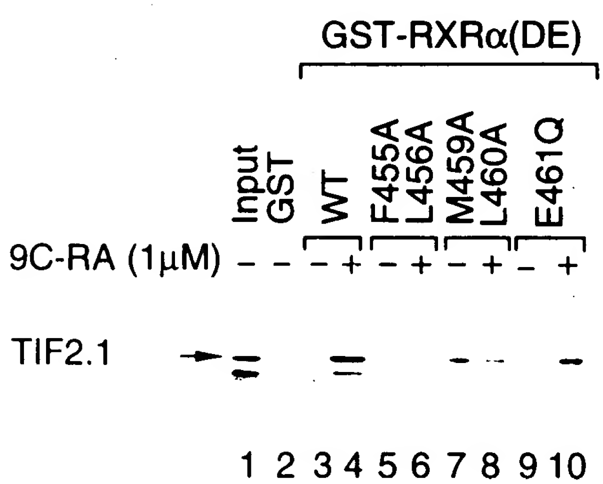

FIG.4M

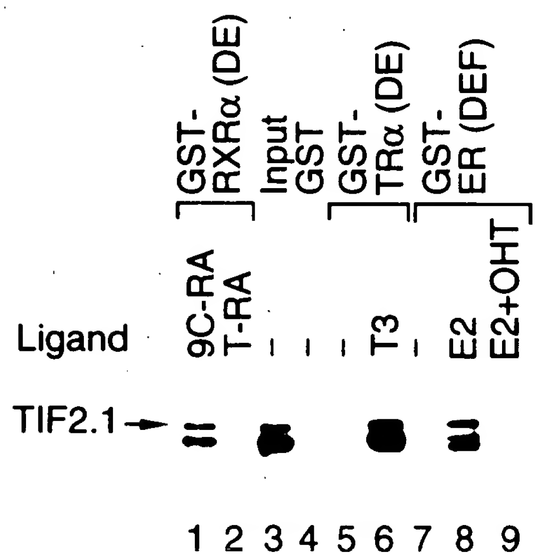

FIG.4N

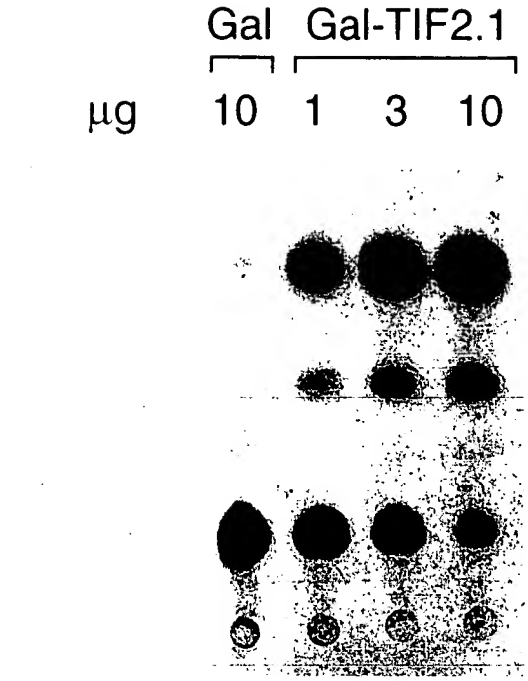

FIG.5A

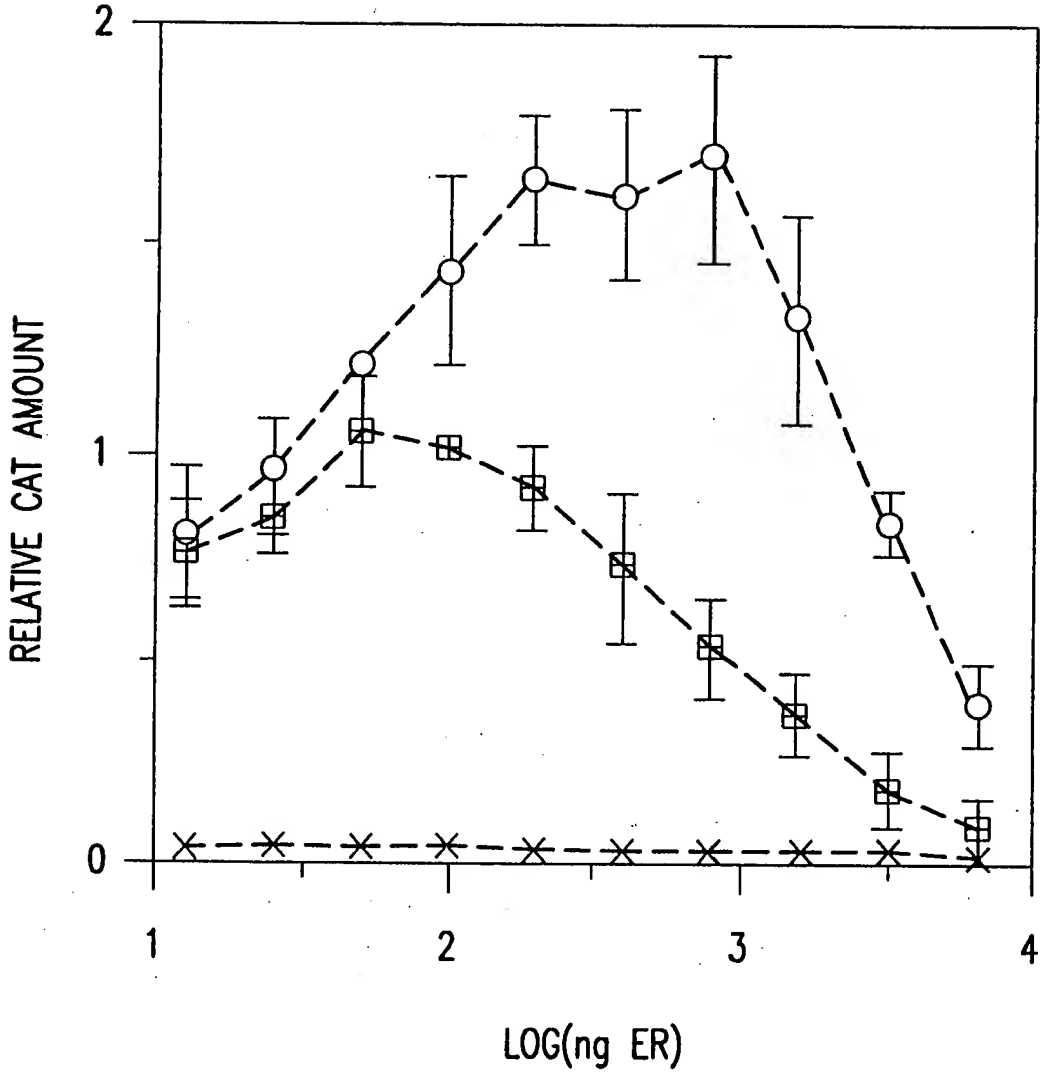

FIG.5B

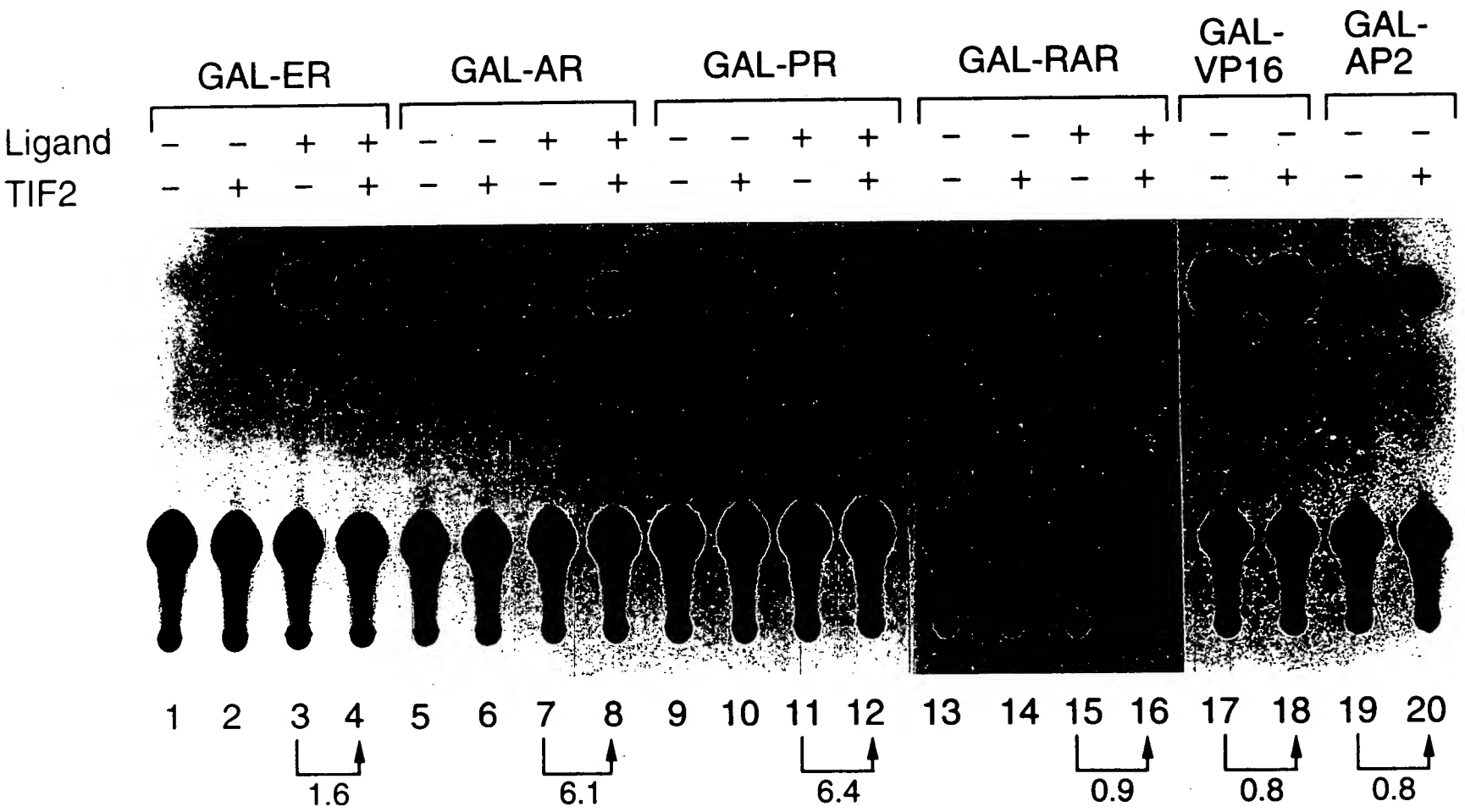

FIG.5C

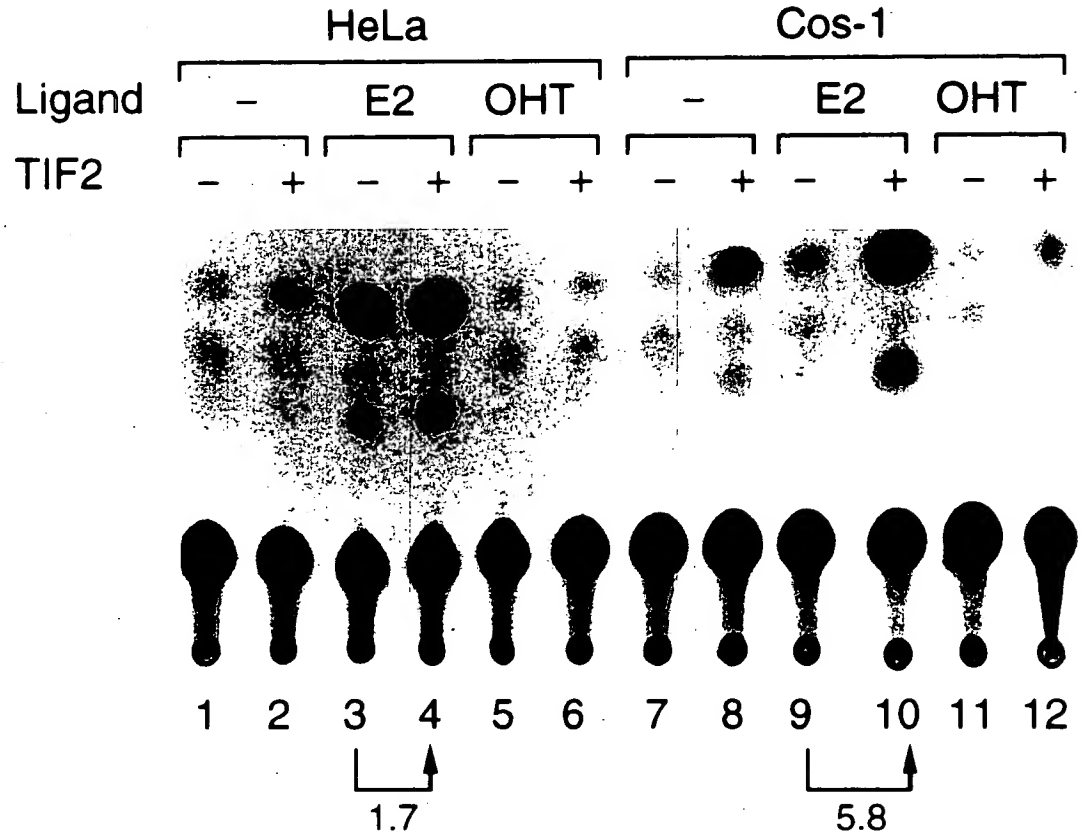

FIG.5E

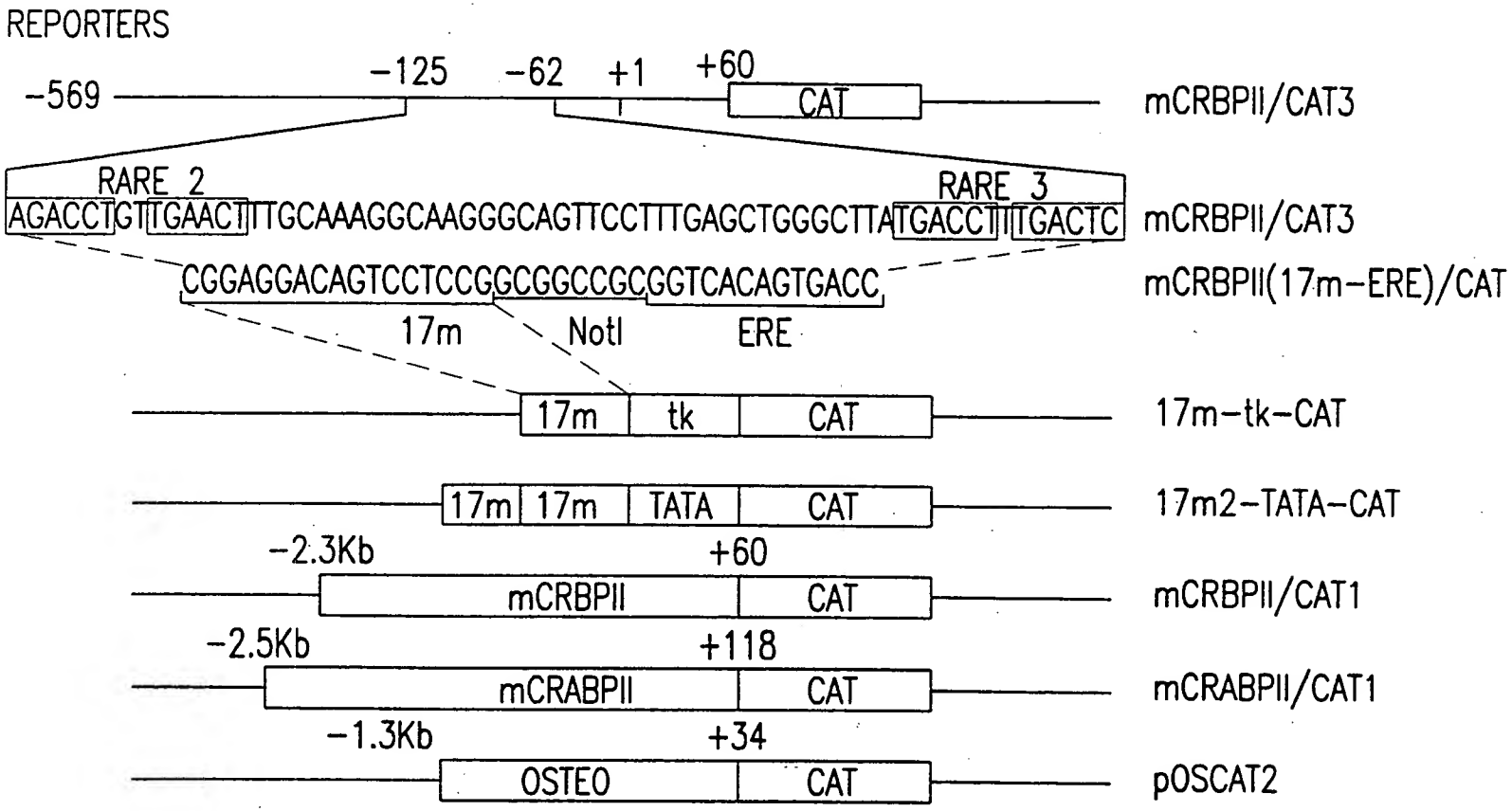
REPORTERS
-569
-125
-62
+1
+60
CAT
mCRBPII/CAT3
RARE 2
RARE 3
AGACCTGTTGAACTTTGCAAAGGCAAGGGCAGTTCCTTTGAGCTGGGCTTATGACCTTTGACTC
mCRBPII/CAT3
CGGAGGACAGTCCTCCGGCGGCCGCGGTCACAGTGACC
mCRBPII(17m-ERE)/CAT
17m
NotI
ERE
17m
tk
CAT
17m-tk-CAT
17m
17m
TATA
CAT
17m2-TATA-CAT
-2.3Kb
+60
mCRBPII
CAT
mCRBPII/CAT1
-2.5Kb
+118
mCRABPII
CAT
mCRABPII/CAT1
-1.3Kb
+34
OSTEO
CAT
pOSCAT2

FIG.6A

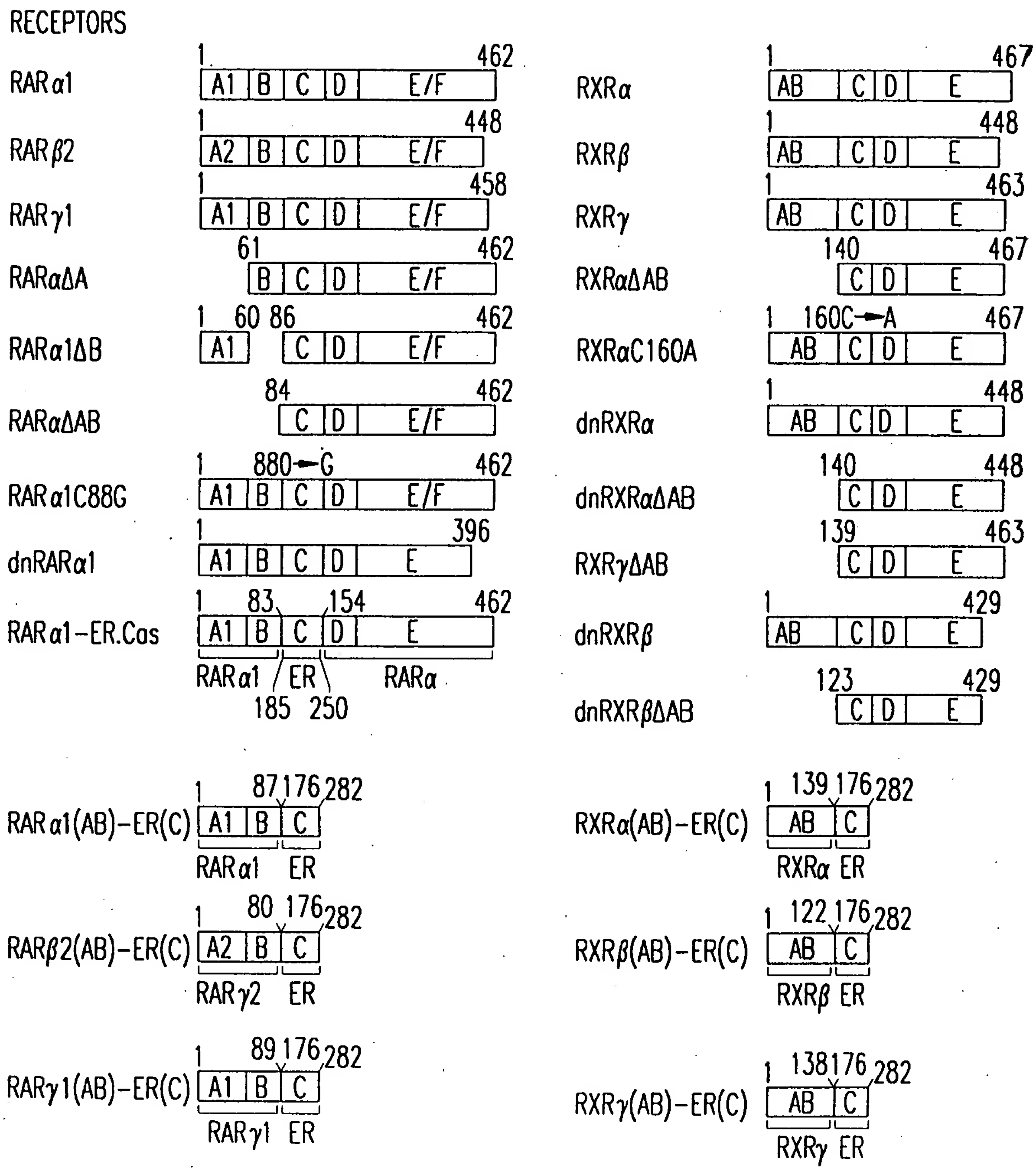
RECEPTORS
RARα1
RARβ2
RARγ1
RARαΔA
RARα1ΔB
RARαΔAB
RARα1C88G
dnRARα1
RARα1-ER.Cas
RXRα
RXRβ
RXRγ
RXRαΔAB
RXRαC160A
dnRXRα
dnRXRαΔAB
RXRγΔAB
dnRXRβ
dnRXRβΔAB
RARα1(AB)-ER(C)
RARβ2(AB)-ER(C)
RARγ1(AB)-ER(C)
RXRα(AB)-ER(C)
RXRβ(AB)-ER(C)
RXRγ(AB)-ER(C)
A1
A2
AB
B
C
D
E
E/F
ER
RARα1
RARα
RARγ2
RARγ1
RXRα
RXRβ
RXRγ
880→G
160C→A
185 250

FIG.6B

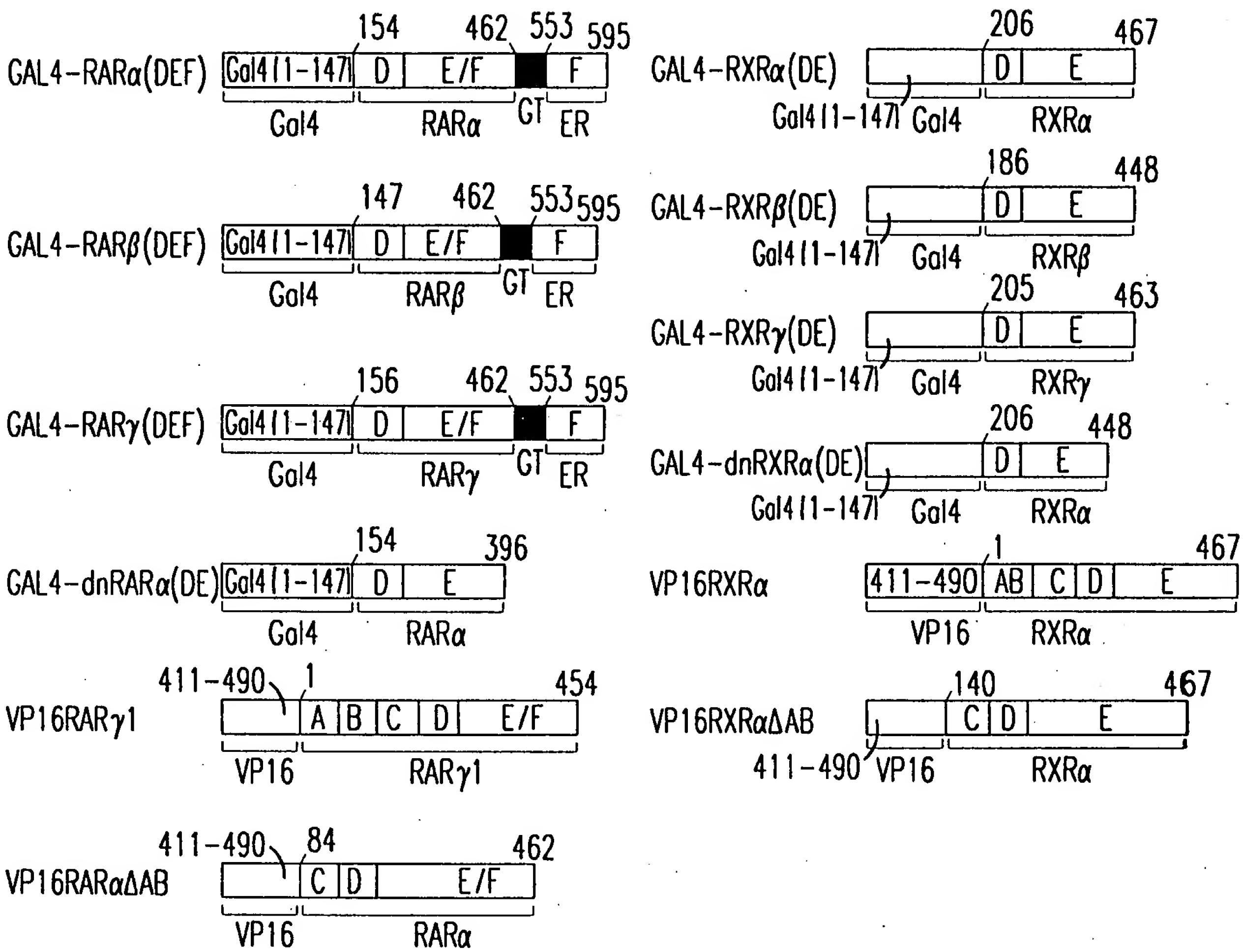
GAL4-RARα(DEF)
154
462
553
595
Gal4(1-147)
D
E/F
F
Gal4
RARα
GT
ER
GAL4-RARβ(DEF)
147
462
553
595
Gal4(1-147)
D
E/F
F
Gal4
RARβ
GT
ER
GAL4-RARγ(DEF)
156
462
553
595
Gal4(1-147)
D
E/F
F
Gal4
RARγ
GT
ER
GAL4-dnRARα(DE)
154
396
Gal4(1-147)
D
E
Gal4
RARα
VP16RARγ1
411-490
1
454
A
B
C
D
E/F
VP16
RARγ1
VP16RARαΔAB
411-490
84
462
C
D
E/F
VP16
RARα
GAL4-RXRα(DE)
206
467
D
E
Gal4(1-147)
Gal4
RXRα
GAL4-RXRβ(DE)
186
448
D
E
Gal4(1-147)
Gal4
RXRβ
GAL4-RXRγ(DE)
205
463
D
E
Gal4(1-147)
Gal4
RXRγ
GAL4-dnRXRα(DE)
206
448
D
E
Gal4(1-147)
Gal4
RXRα
VP16RXRα
1
467
411-490
AB
C
D
E
VP16
RXRα
VP16RXRαΔAB
140
467
C
D
E
411-490
VP16
RXRα

FIG.6C

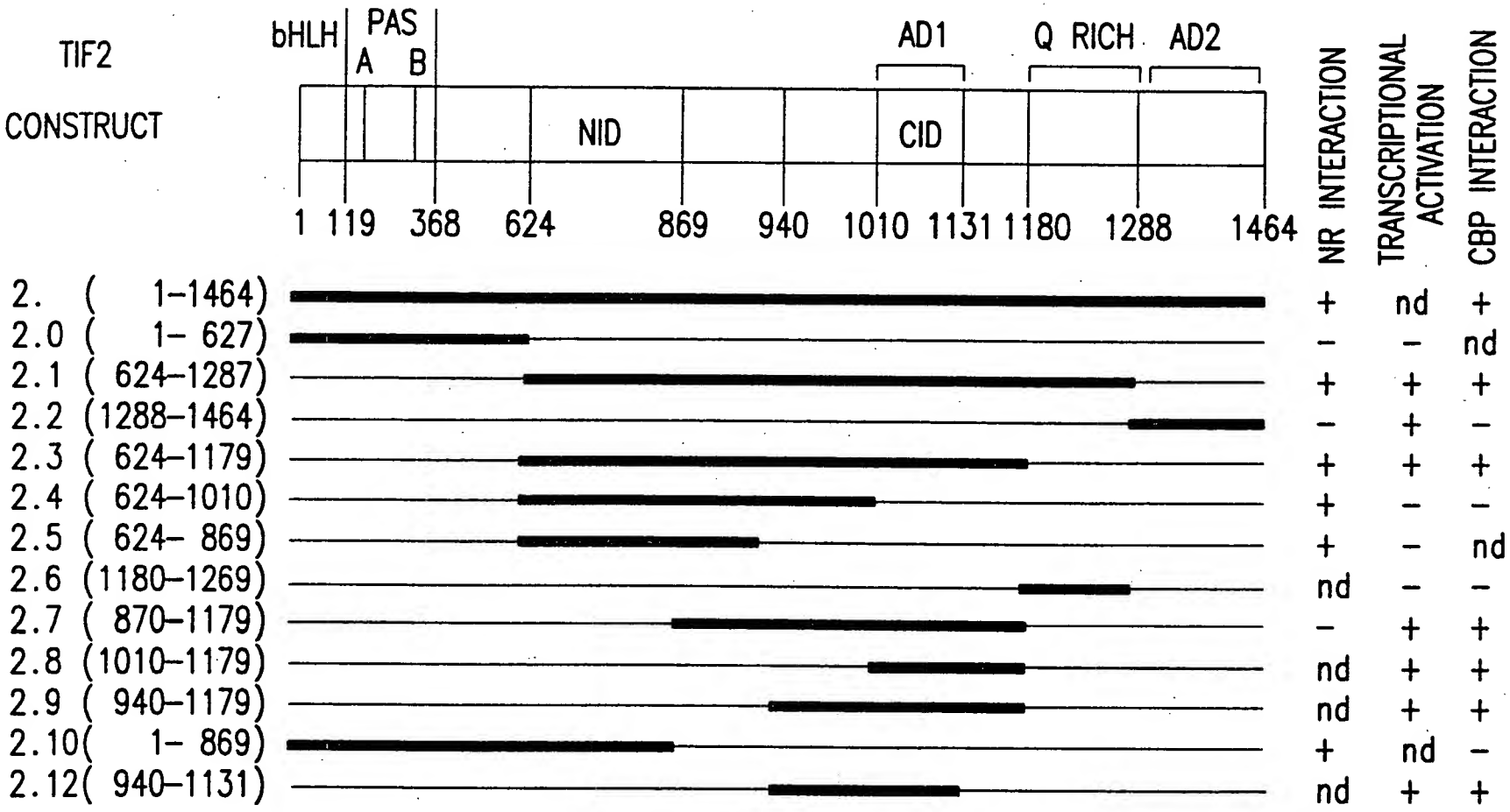

FIG.7A

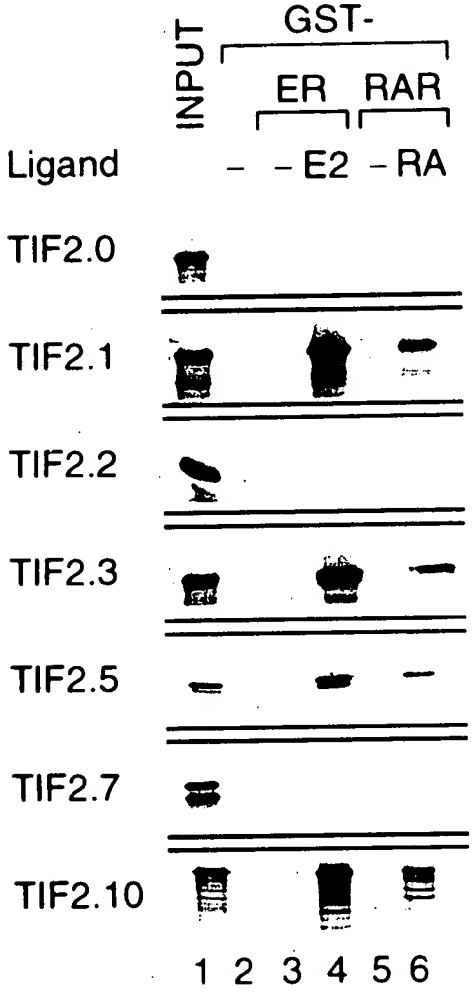
INPUT
GST-
ER
RAR
Ligand
– – E2 – RA
TIF2.0
TIF2.1
TIF2.2
TIF2.3
TIF2.5
TIF2.7
TIF2.10
1 2 3 4 5 6

FIG.7B


INPUT
GST
GST-CBP*
TIF2.1
TIF2.2
TIF2.3
TIF2.4
TIF2.6
TIF2.7
TIF2.8
TIF2.9
TIF2.10
TIF2.12
1 2 3

FIG.7D

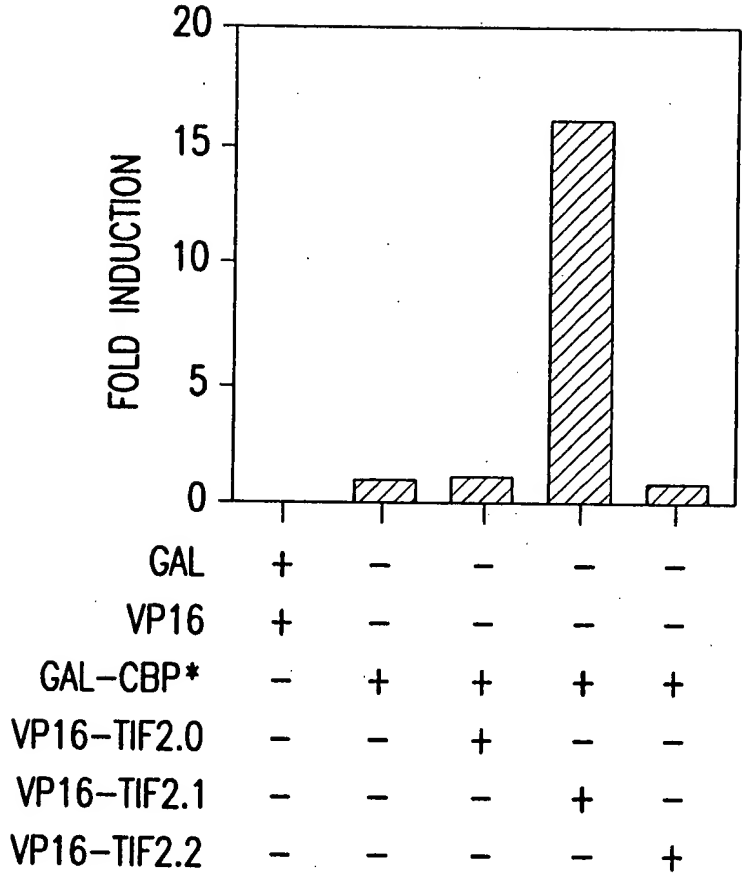
20
15
10
5
0
FOLD INDUCTION
GAL + – – – –
VP16 + – – – –
GAL–CBP* – + + + +
VP16–TIF2.0 – – + – –
VP16–TIF2.1 – – – + –
VP16–TIF2.2 – – – – +

FIG.7E

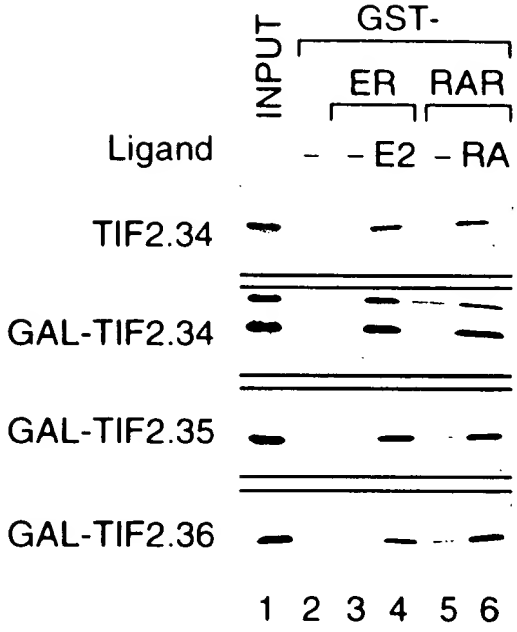

FIG.8C

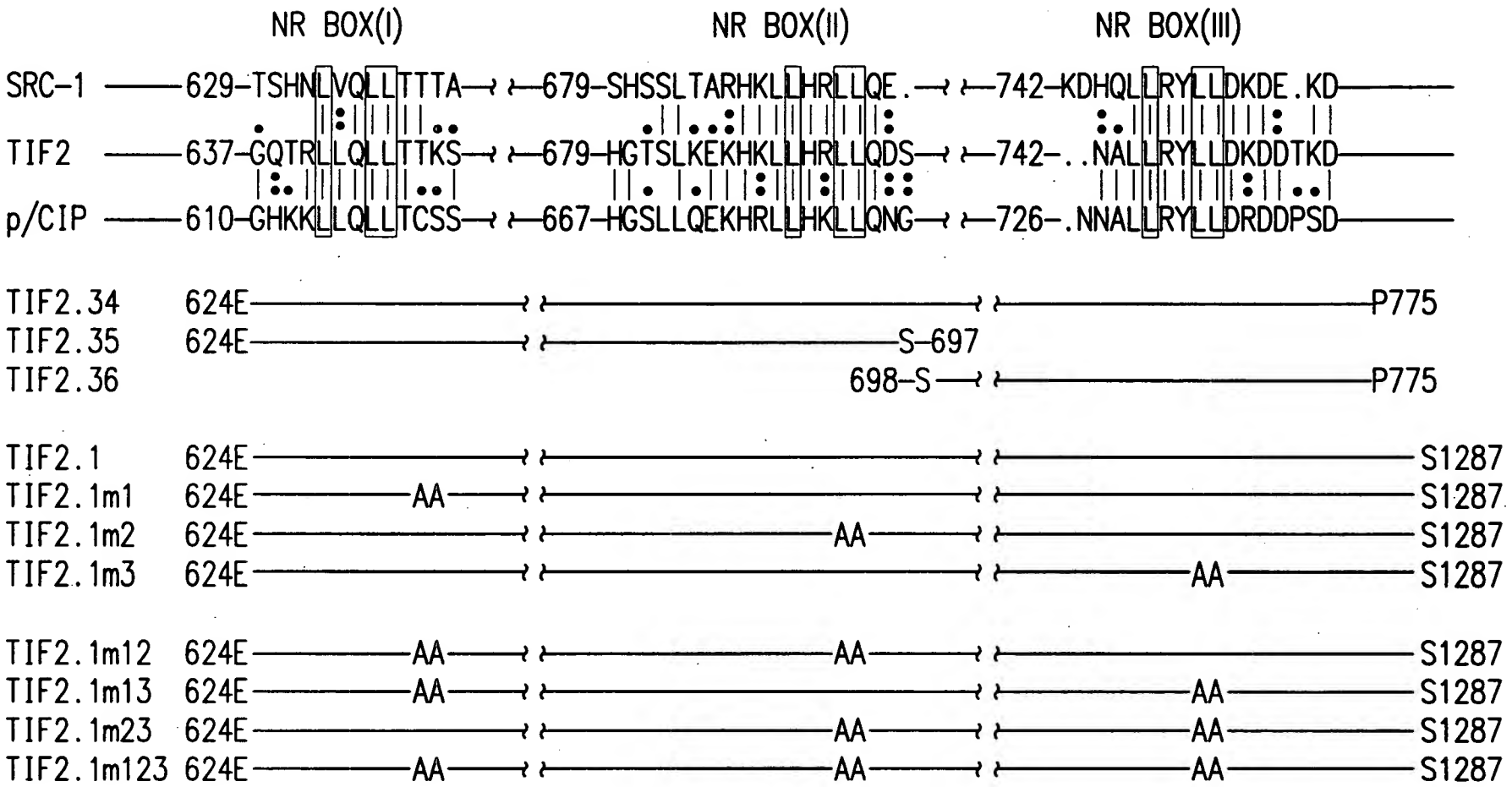
NR BOX(I)
NR BOX(II)
NR BOX(III)
SRC-1 629-TSHNLVQLLTTTA 679-SHSSLTARHKLLHRLLQE. 742-KDHQLLRYLLDKDE.KD
TIF2 637-GQTRLLQLLTTKS 679-HGTSLKEKHKLLHRLLQDS 742-..NALLRYLLDKDDTKD
p/CIP 610-GHKKLLQLLTCSS 667-HGSLLQEKHRLLHKLLQNG 726-.NNALLRYLLDRDDPSD
TIF2.34 624E P775
TIF2.35 624E S-697
TIF2.36 698-S P775
TIF2.1 624E S1287
TIF2.1m1 624E AA S1287
TIF2.1m2 624E AA S1287
TIF2.1m3 624E AA S1287
TIF2.1m12 624E AA AA S1287
TIF2.1m13 624E AA AA S1287
TIF2.1m23 624E AA AA S1287
TIF2.1m123 624E AA AA AA S1287

FIG.8A

NR box

TIF1α	724	– RSILTSLLLNSS –	735
RIP140	933	– FNVLKQLLLSEN –	944
TRIP3	95	– SATLRSLLLNPH –	106
TIF2(I)	638	– QTKLLQLLTTKS –	648
TIF2(II)	687	– HKILHRLLQDSS –	698
TIF2(III)	742	– NALLRYLLDKDD –	753

FIG.8B

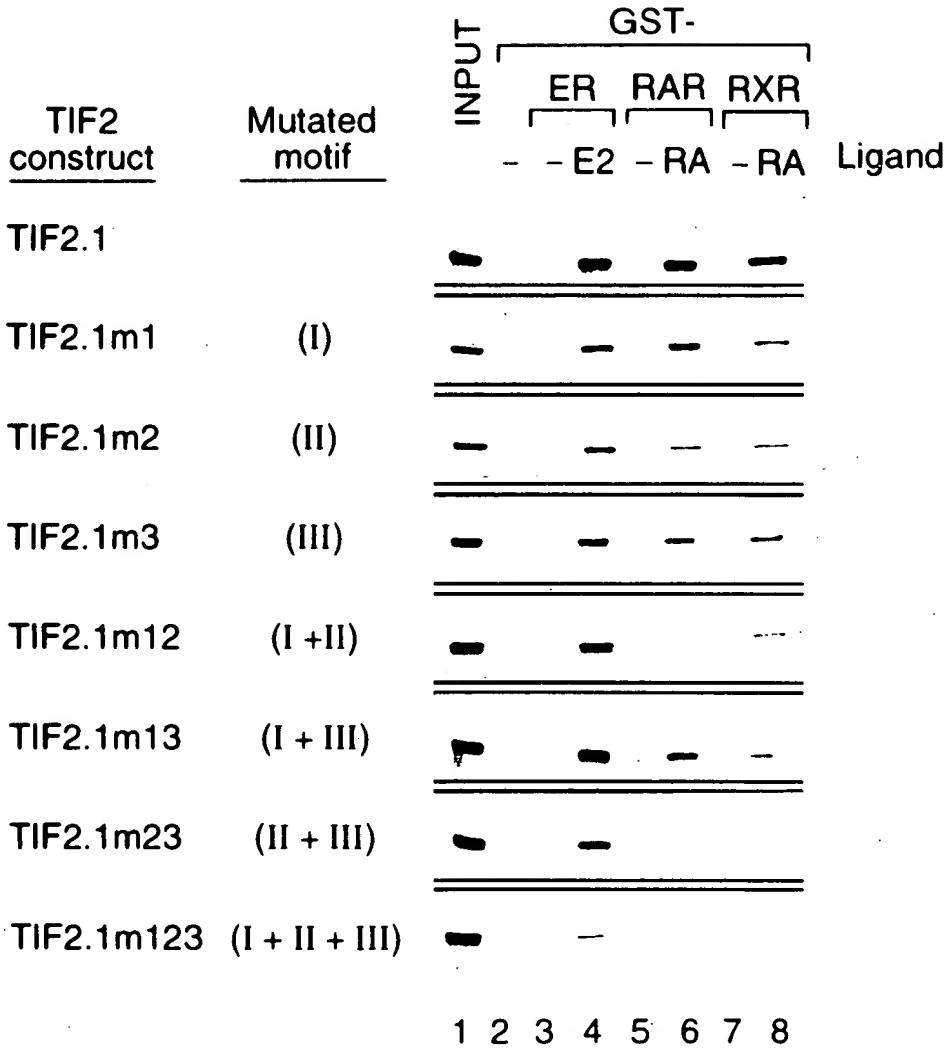

FIG.8D

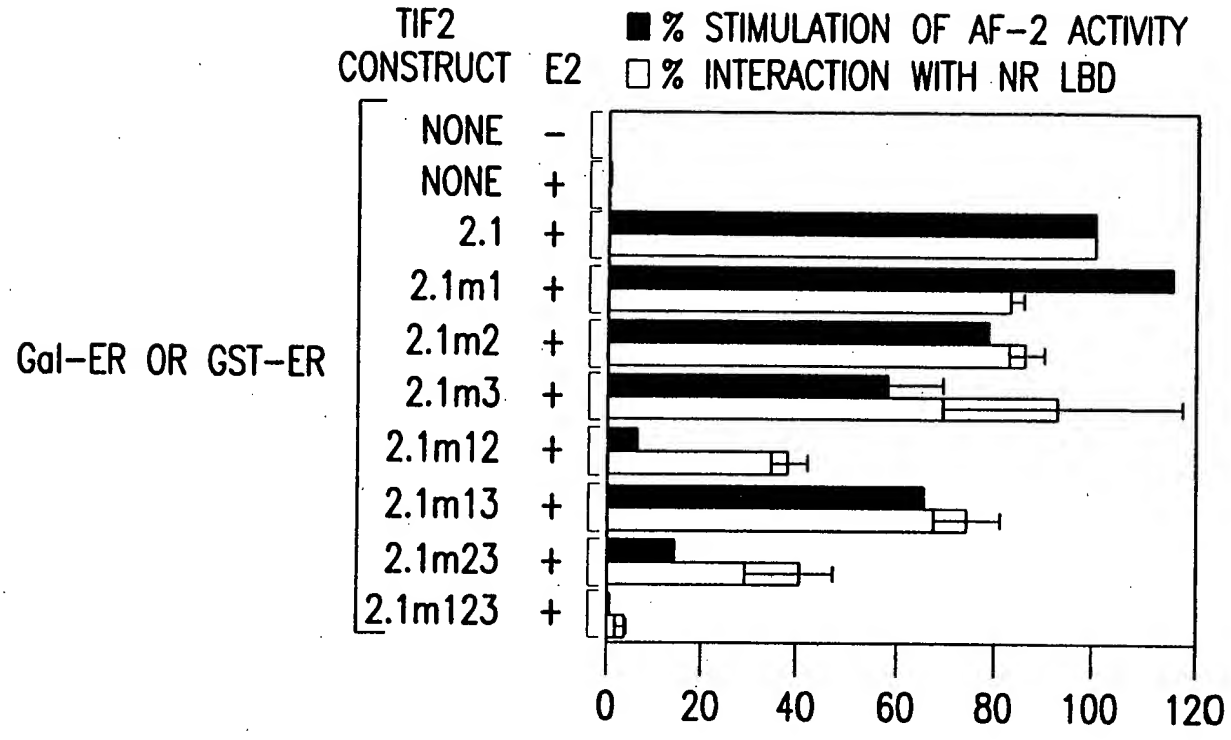
TIF2
CONSTRUCT
E2
% STIMULATION OF AF-2 ACTIVITY
% INTERACTION WITH NR LBD
Gal-ER OR GST-ER
NONE
NONE
2.1
2.1m1
2.1m2
2.1m3
2.1m12
2.1m13
2.1m23
2.1m123
0
20
40
60
80
100
120

FIG.8E

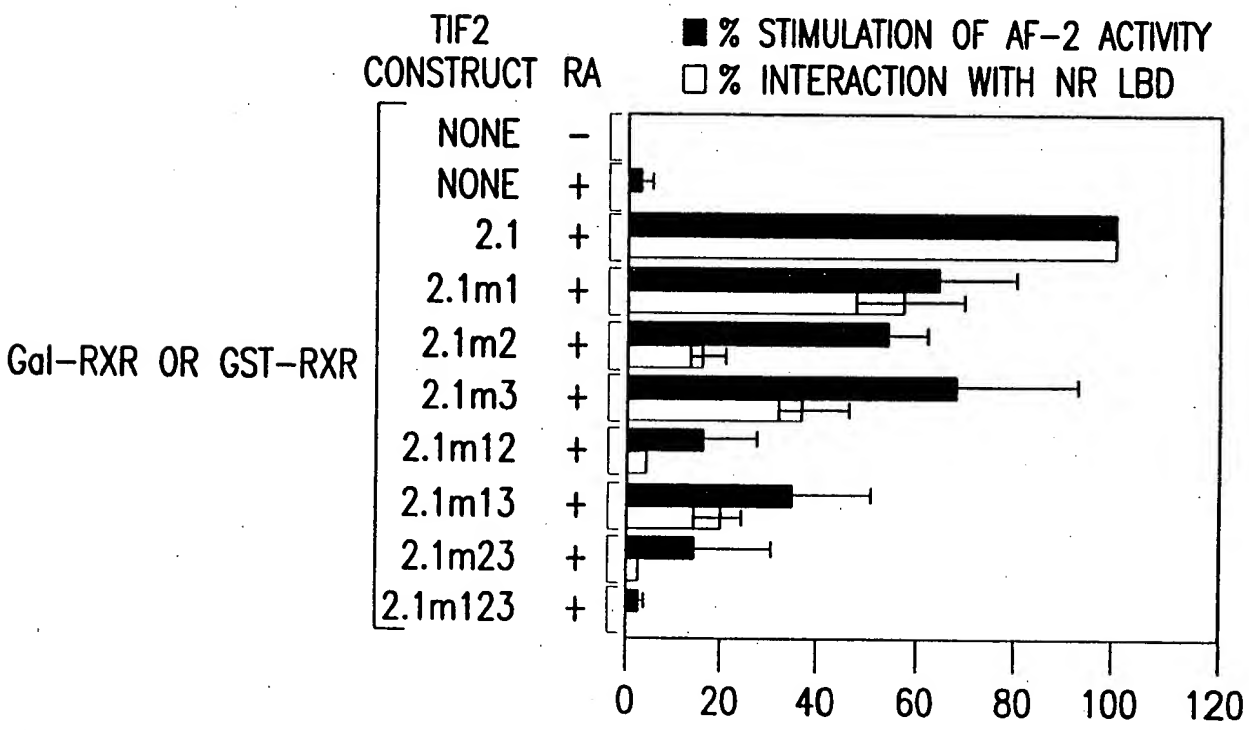
TIF2
CONSTRUCT
RA
% STIMULATION OF AF-2 ACTIVITY
% INTERACTION WITH NR LBD
Gal-RXR OR GST-RXR
NONE
NONE
2.1
2.1m1
2.1m2
2.1m3
2.1m12
2.1m13
2.1m23
2.1m123
0
20
40
60
80
100
120

FIG.8F

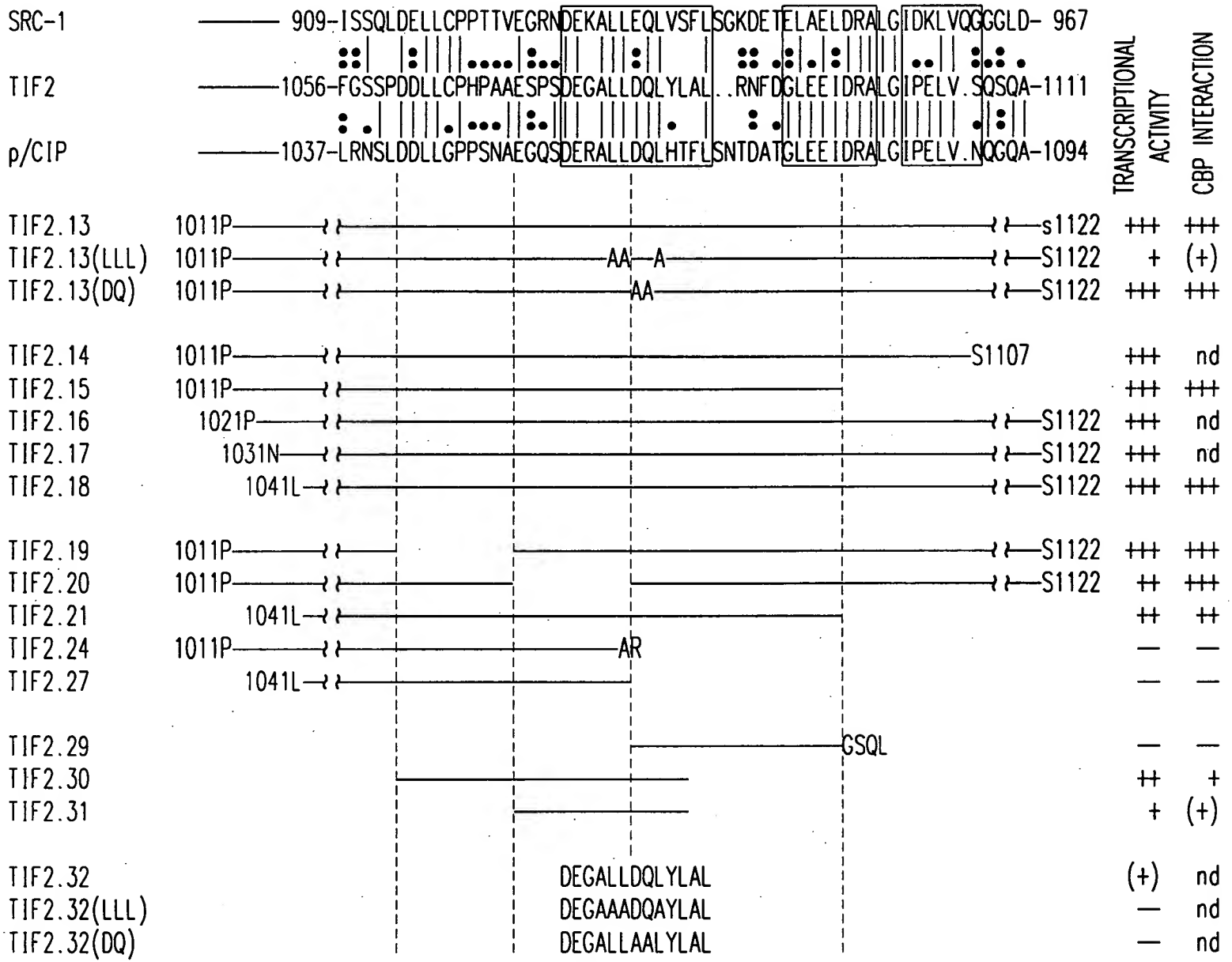
SRC-1 909-ISSQLDELLCPPTTVEGRNDEKALLEQLVSFLSGKDETELAELDRALGIDKLVQGGGLD- 967
TIF2 1056-FGSSPDDLLCPHPAAESPSDEGALLDQLYLAL..RNFDGLEEIDRALGIPELV.SQSQA-1111
p/CIP 1037-LRNSLDDLLGPPSNAEGQSDERALLDQLHTFLSNTDATGLEEIDRALGIPELV.NQGQA-1094
TRANSCRIPTIONAL ACTIVITY
CBP INTERACTION
TIF2.13 1011P s1122 +++ +++
TIF2.13(LLL) 1011P AA A S1122 + (+)
TIF2.13(DQ) 1011P AA S1122 +++ +++
TIF2.14 1011P S1107 +++ nd
TIF2.15 1011P +++ +++
TIF2.16 1021P S1122 +++ nd
TIF2.17 1031N S1122 +++ nd
TIF2.18 1041L S1122 +++ +++
TIF2.19 1011P S1122 +++ +++
TIF2.20 1011P S1122 ++ +++
TIF2.21 1041L ++ ++
TIF2.24 1011P AR — —
TIF2.27 1041L — —
TIF2.29 GSQL — —
TIF2.30 ++ +
TIF2.31 + (+)
TIF2.32 DEGALLDQLYLAL (+) nd
TIF2.32(LLL) DEGAAADQAYLAL — nd
TIF2.32(DQ) DEGALLAALYLAL — nd

FIG.9A

GAL-TIF	Fold Induction of (17m)5-TATA-CAT	
	Cos-1	HeLa
2.13	462 ± 9	704 ± 33
2.14	392 ± 13	674 ± 23
2.15	279 ± 21	316 ± 49
2.16	390 ± 34	597 ± 54
2.17	389 ± 50	581 ± 58
2.18	314 ± 16	432 ± 19
2.19	341 ± 67	777 ± 30
2.20	107 ± 11	314 ± 27
2.21	129 ± 8	173 ± 22
2.24	< 2	< 2
2.27	< 2	< 2
2.29	< 2	< 2
2.30	98 ± 13	117 ± 6
2.31	35 ± 3	34 ± 3
2.32	2.8 ± 0.2	5.9 ± 0.9
2.32(LLL)	1.4 ± 0.2	1.5 ± 0.1
2.32(DQ)	1.7 ± 0.3	1.2 ± 0.2

FIG.9B

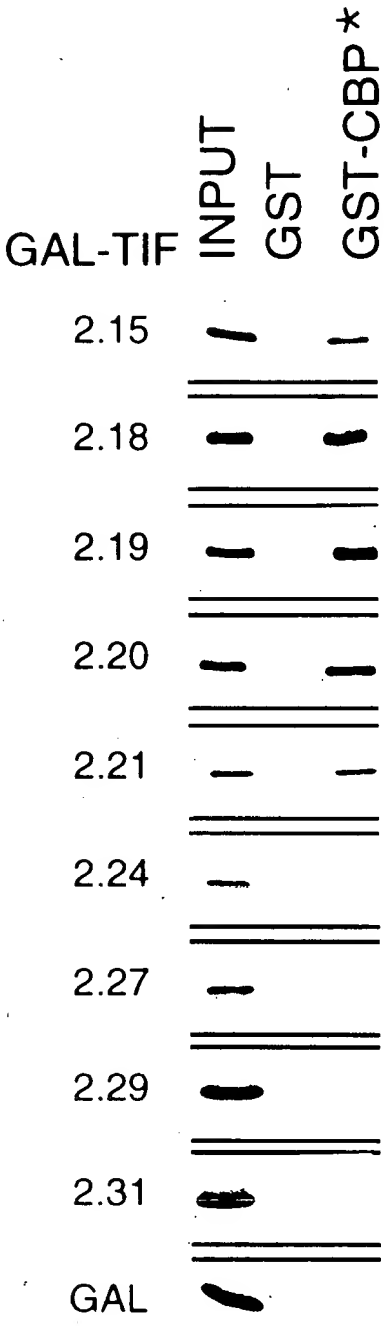

FIG.9C

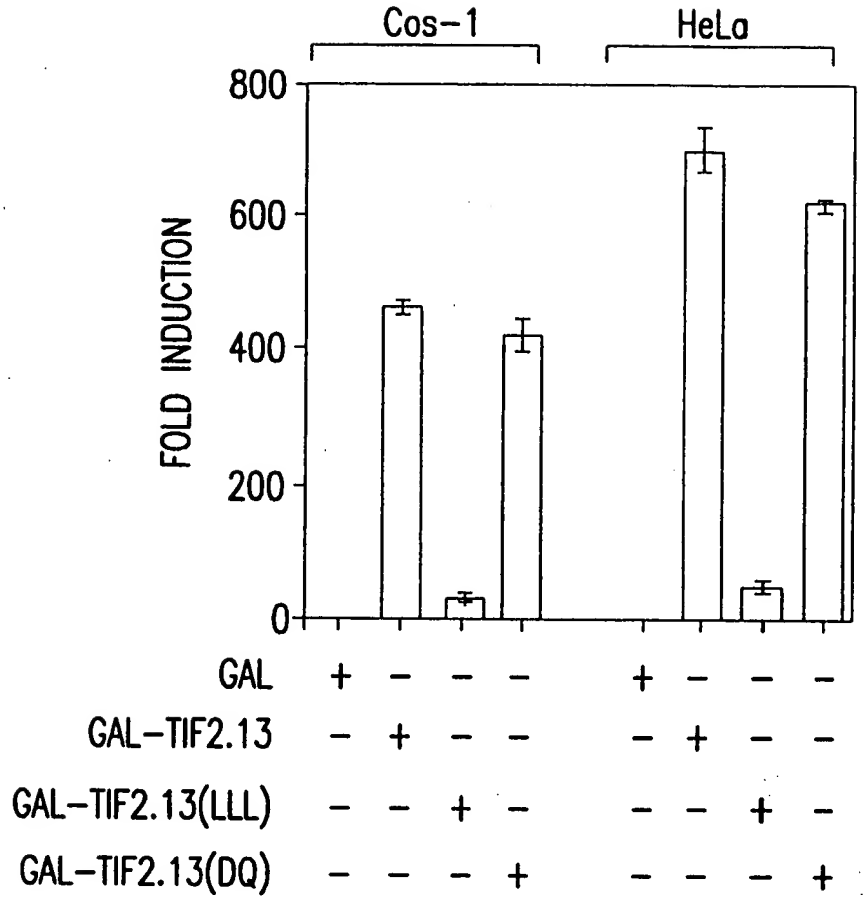

FIG.10A

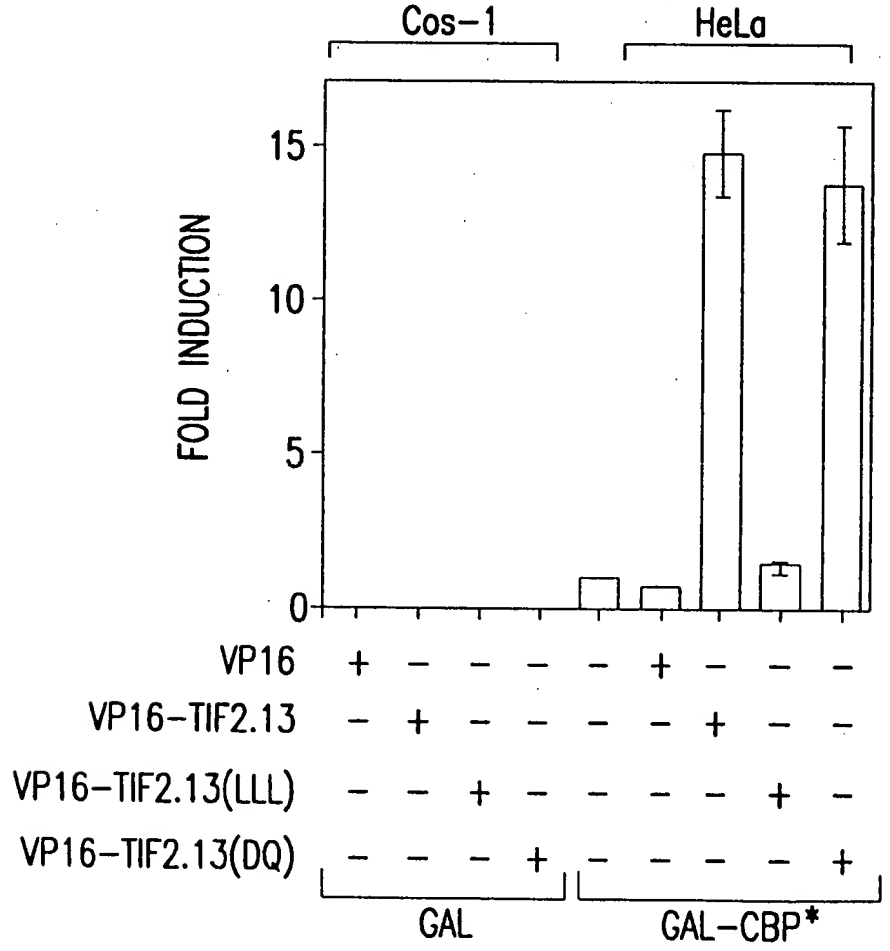

FIG.10B

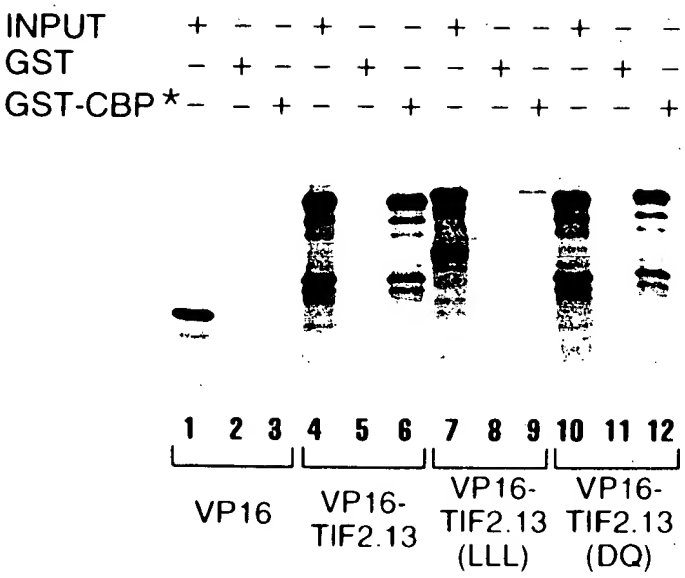

FIG.10C

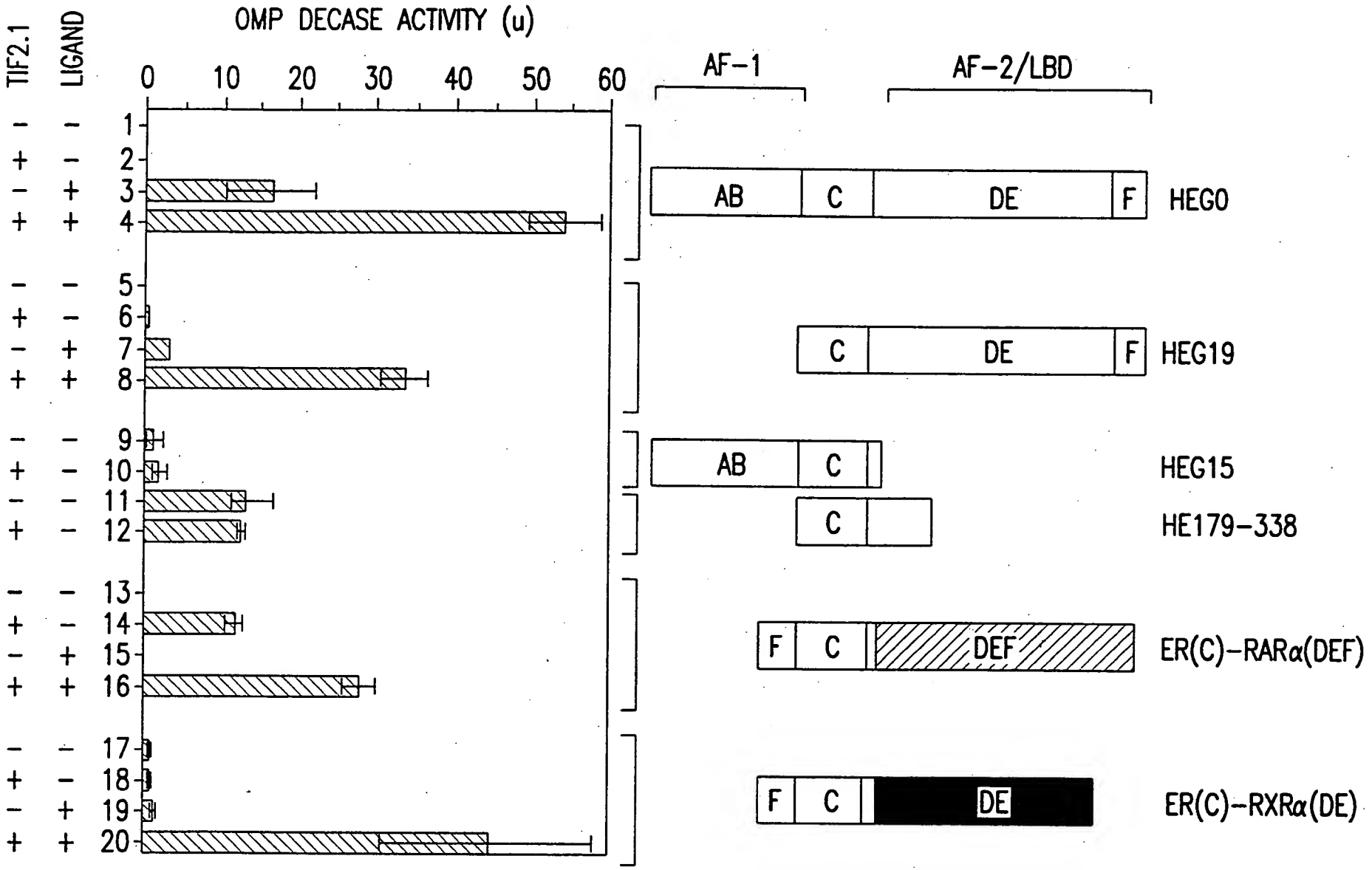
OMP DECASE ACTIVITY (u)
0
10
20
30
40
50
60
TIF2.1
LIGAND
AF-1
AF-2/LBD
AB
C
DE
F
HEG0
HEG19
HEG15
HE179-338
DEF
ER(C)-RARα(DEF)
ER(C)-RXRα(DE)

FIG.11

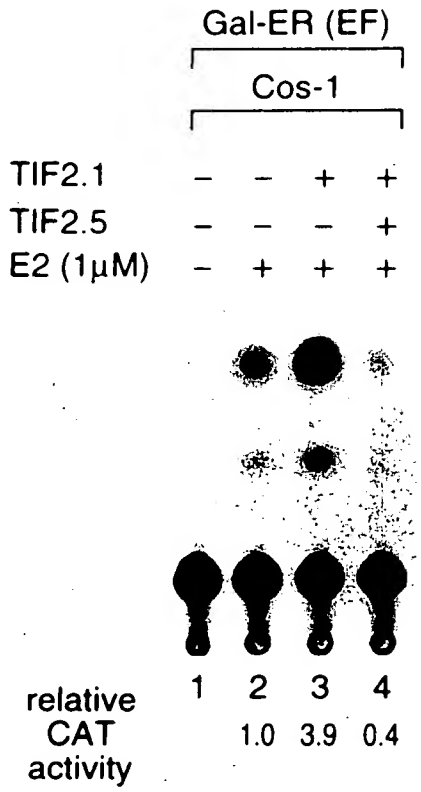

FIG.12A

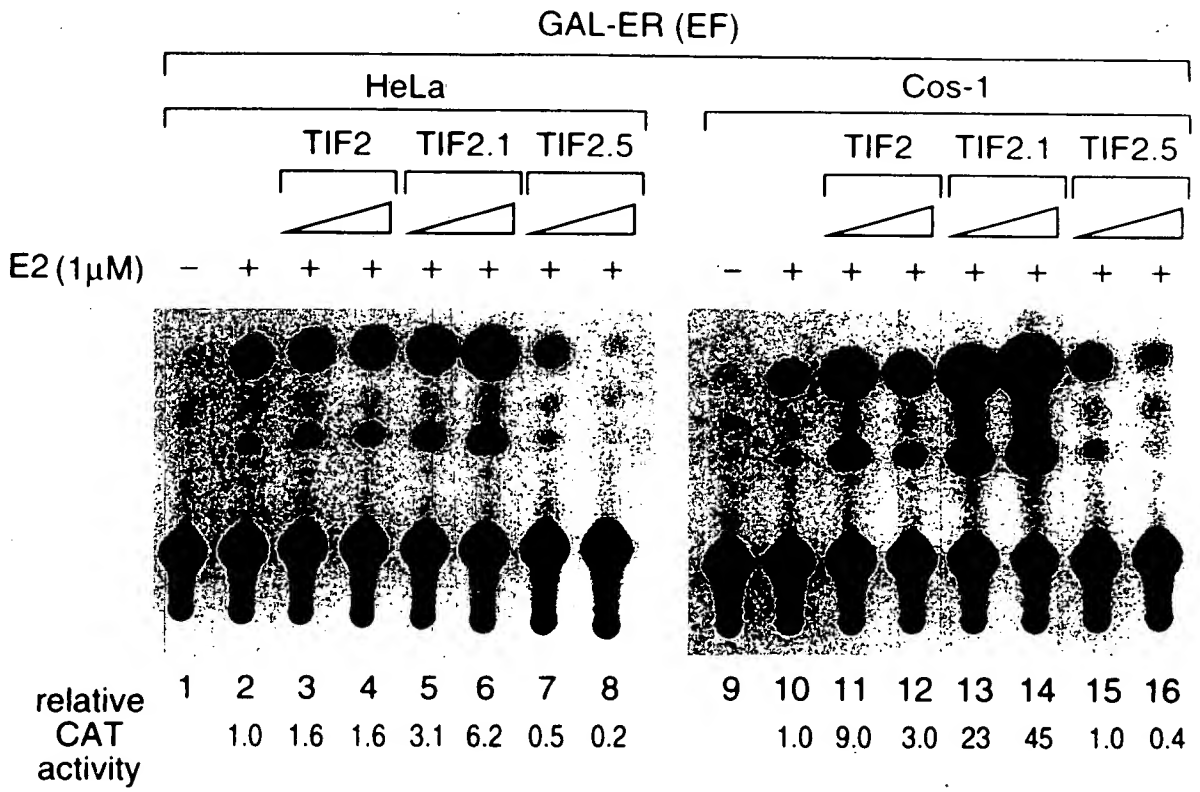

FIG.12B

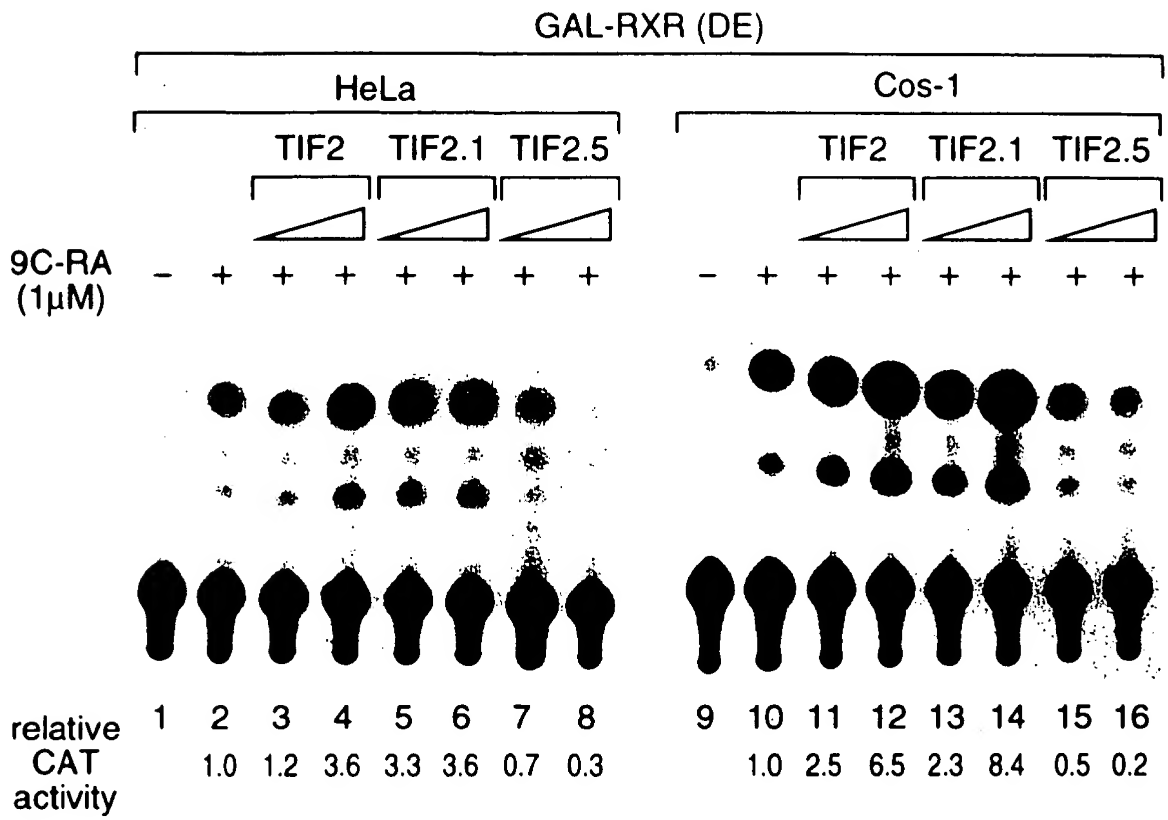

FIG.12C

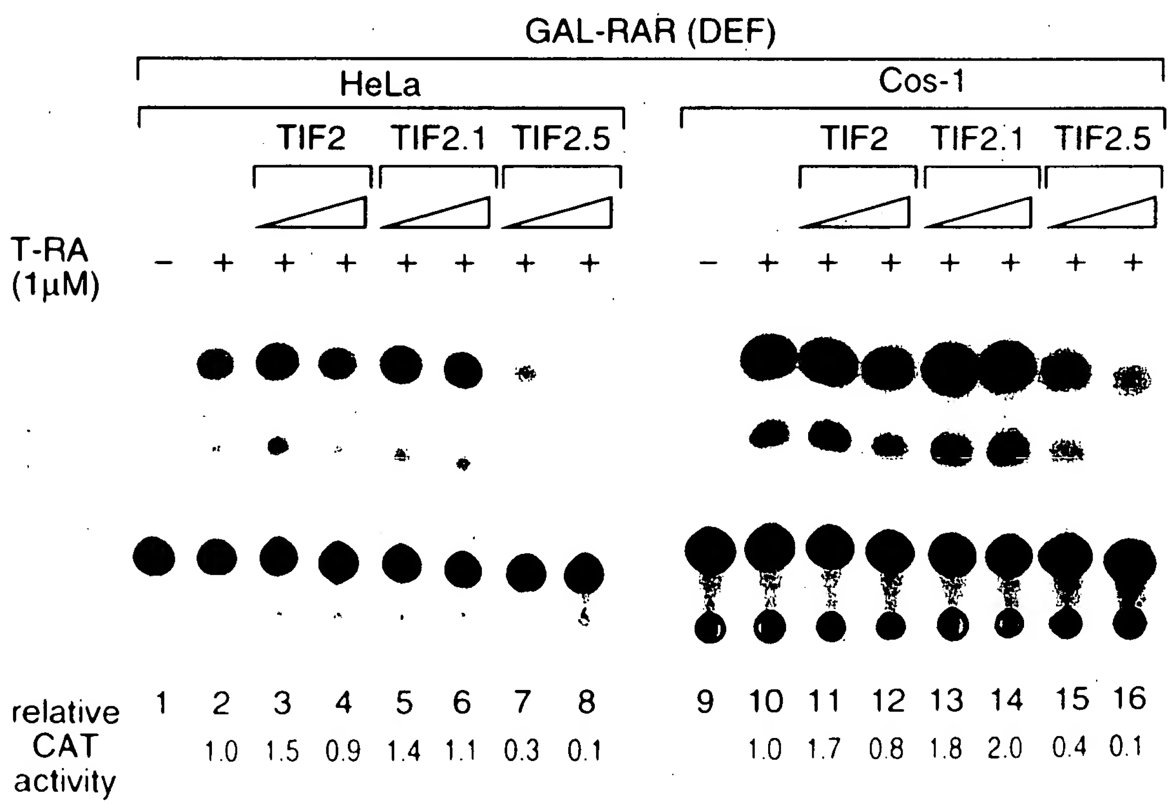

FIG.12D